

1 agggagagggc agtgaccatg aaggctgtgc tgcctgccc tttgattggca
 51 ggcttggccc tgcagccagg cactgcccctg ctgtgctact cctgcaaagc
 101 ccaggtgagc aacgaggact gccctgcaggt ggagaactgc acccagctgg
 151 gggagcagtg ctggaccgcg cgcatccgcg cagtggcct cctgaccgtc
 201 atcagcaaag gctgcagctt gaactgcgtg gatgactcac aggactacta
 251 cgtgggcaag aagaacatca cgtgctgtga caccgacttg tgcaacgcca
 301 gcgggggccc tgcctgcag ccggctgccg ccatcctgc gctgctccct
 351 gcactcggcc tgcctgctctg gggaccggc cagctatagg ctctgggggg
 401 ccccgctgca gccacactg ggtgtgtgc cccaggcctt tgtgccactc
 451 ctacagaac ctggcccagt gggagcctgt cctggctcct gaggcacatc
 501 ctaacgcaag ttgaccatg tatgttgca cccctttcc cnaaccctg
 551 acctcccat gggcctttc caggattccn accnggcaga tcagtttag
 601 tganacanat ccgctgcag atggccctc caacnnttn tgttgnntn
 651 tccatggccc agcatttcc accttaacc ctgtgtcag gcactnncc
 701 cccaggaag cctccctgc ccacccan tatgaattga gccaggttg
 751 gtccgtgtg tccccgcac ccagcagggg acaggcaatc aggaggggcc
 801 agtaagggc gagatgaagt ggactgagta gaactggagg acaagagntg
 851 acgtgagntc ctgggagntt ccagagatgg ggcctggagg cctggaggaa
 901 gggggccaggc ctacatntg tggggnccc gaatggcagc ctgagcaccg
 951 cgtaggccct taataaacac ctgntgata agccaaaaaa aaaaaaaa

FIGURE 1A

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0094773-083101

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1  ATGAAGACAGTTTTTTTTATCCTGCTGGCCACCTACTTAGCCCTGCATCCAGGTGCTGCT 60
   TACTTCTGTCAAAAAAATAGGACGACCGGTGGATGAATCGGGACGTAGGTCCACGACGA
   M K T V F F I L L A T Y L A L H P G A A -
61  CTGCAGTGCTATTTCATGCACAGCACAGATGAACAACAGAGACTGTCTGAATGTACAGAAC 120
   GACGTCACGATAAGTACGTGTCGTGCTACTTGTGTCTCTGACAGACTTACATGTCTTG
   L Q C Y S C T A Q M N N R D C L N V Q N -
121 TGCAGCCTGGACCAGCACAGTTGCTTTACATCGCGCATCCGGGCCATTGGACTCGTGACA 180
   ACGTCGGACCTGGTCGTGTCACGAAATGTAGCGCGTAGGCCCGGTAACCTGAGCACTGT
   C S L D Q H S C F T S R I R A I G L V T -
181 GTTATCAGTAAGGGCTGCAGCTCACAGTGTGAGGATGACTCGGAGAACTACTATTTGGGC 240
   CAATAGTCATTCCCGACGTCGAGTGTACACTCCTACTGAGCCTCTTGATGATAAACCCG
   V I S K G C S S Q C E D D S E N Y Y L G -
241 AAGAAGAACATCACGTGCTGCTACTCTGACCTGTGCAATGTCAACGGGGCCACACCCCTG 300
   TTCTTCTTGTAGTGACGACGATGAGACTGGACACGTTACAGTTGCCCCGGGTGTGGGAC
   K K N I T C C Y S D L C N V N G A H T L -
301 AAGCCACCCACCAACCTGGGGCTGCTGACCGTGCTCTGCAGCCTGTTGCTGTGGGGCTCC 360
   TTCGGTGGGTGGTGGGACCCGACGACTGGCACGAGACGTGGGACAACGACACCCCGAGG
   K P P T T L G L L T V L C S L L L W G S -
361 AGCCGTCTGTAGGCTCTGGGAGAGCCTACCATAGCCCGATTGTGAAGGGATGAGCTGCAC 420
   TCGGCAGACATCCGAGACCCTCTCGGATGGTATCGGGCTAACACTTCCCTACTCGACGTG
   S R L *
421 TCCACCCCAACCCACACAGG 441
   AGGTGGGGTGGGGTGTGTCC
```

FIGURE 2

[Faint, illegible handwritten notes]

FIGURE 3

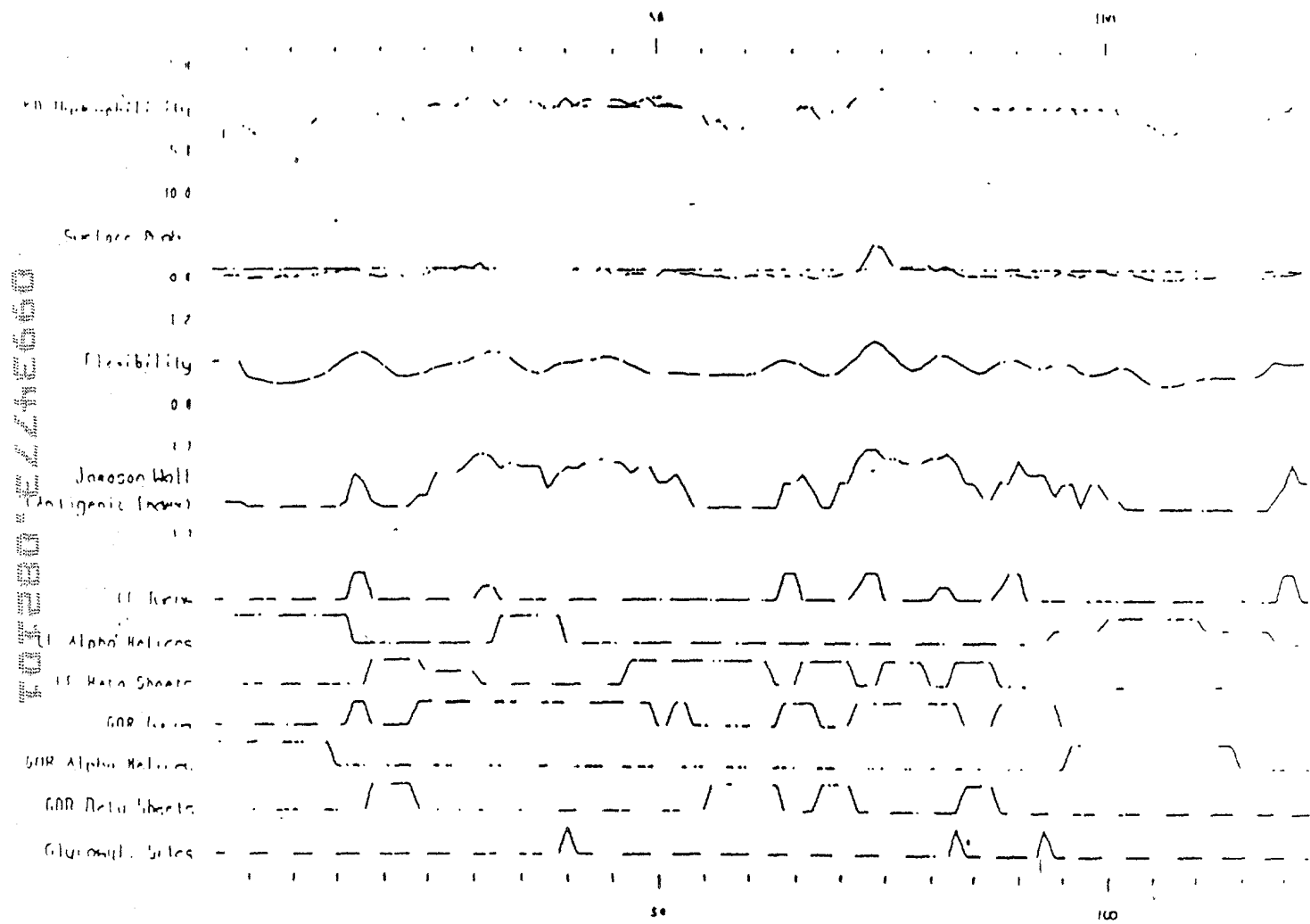


FIGURE 4

09934773 082404

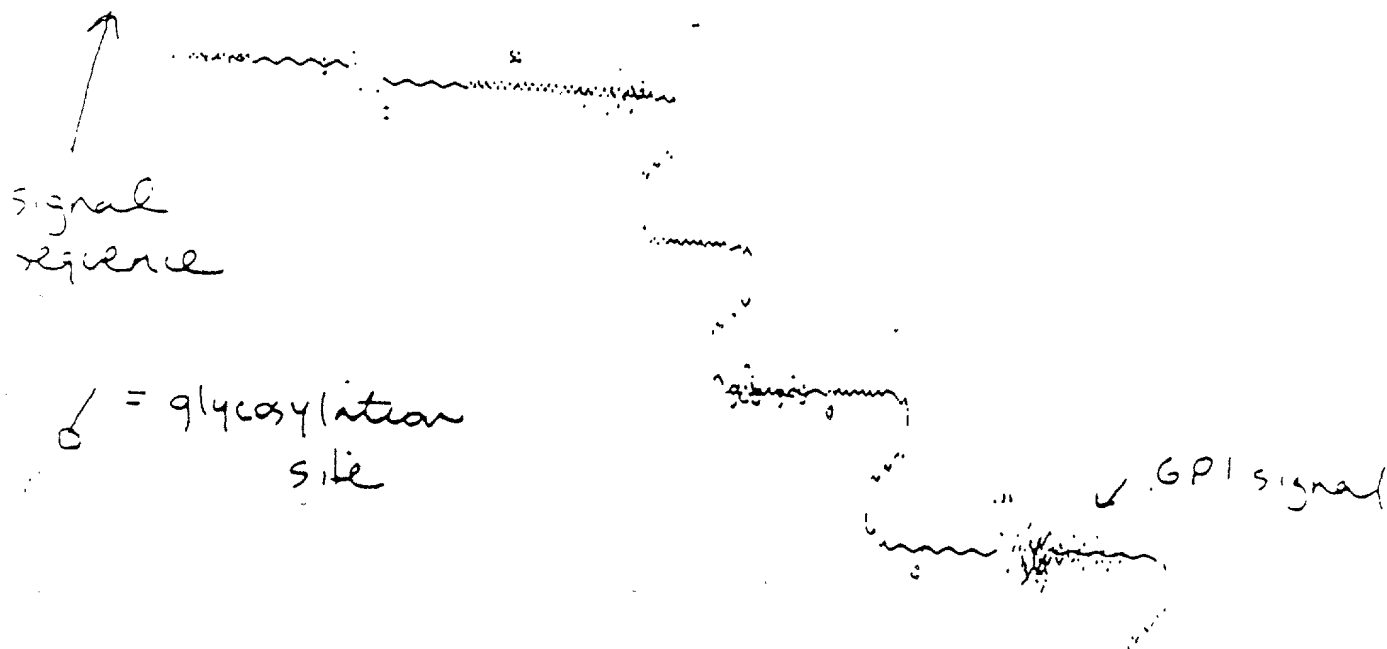
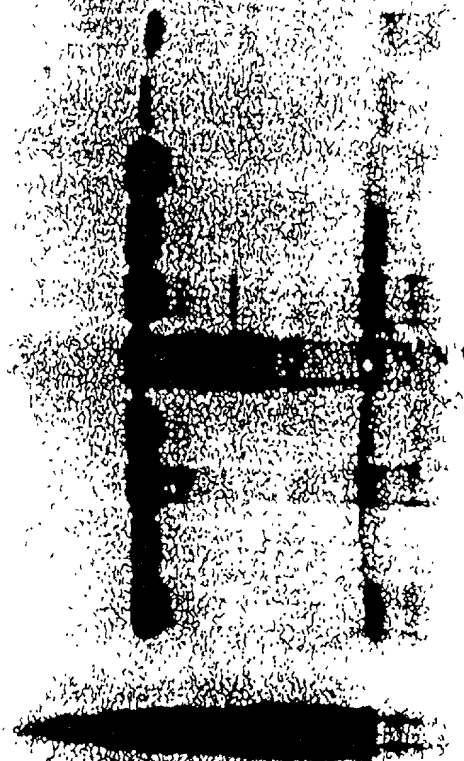


FIGURE 5

Western ASCA
 Superoxide 80mg/ml
 Normal tissue
 1hr exp

1G8
 1:100

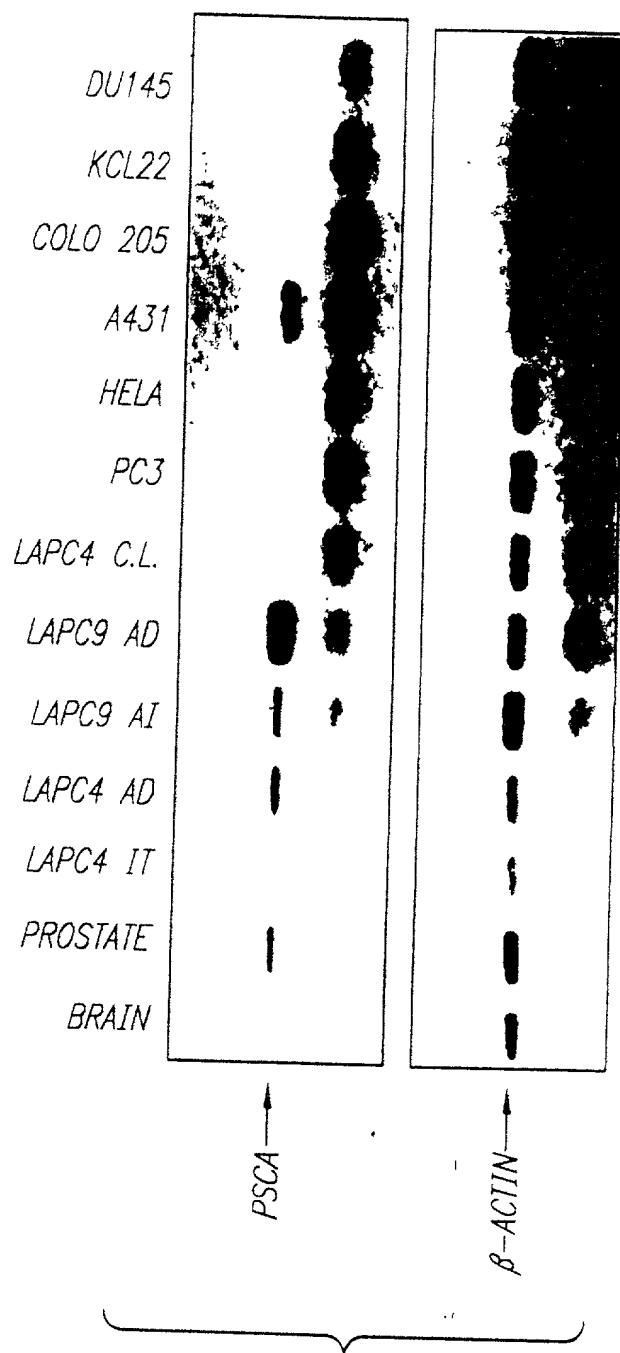
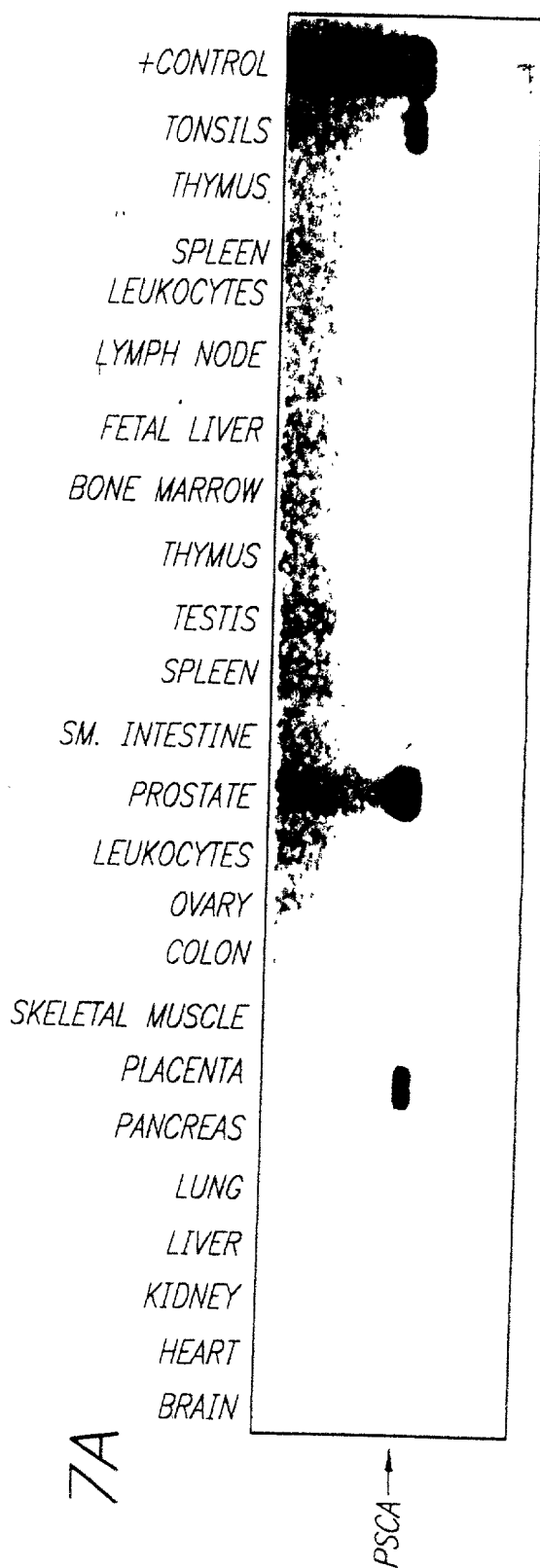


prostate (Kinner)
 prostate (Baker)
 prostate (GCK)
 Bladder (Kinner)
 Bladder (GCK)
 Bladder (Rob)
 Kidney (N404)
 Kidney (W42)
 Testis
 Sm. Intest.

LA PC9

FIGURE 6

09934773.082101



PSCA / PSA Expression in Benign
Prostate vs. Prostate Cancer Xenograft

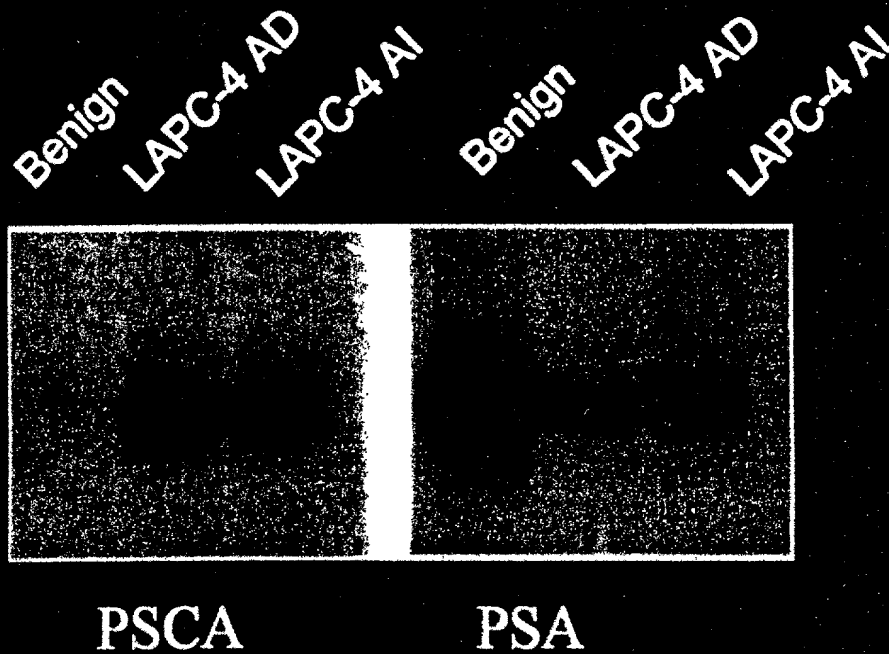


FIGURE 9A

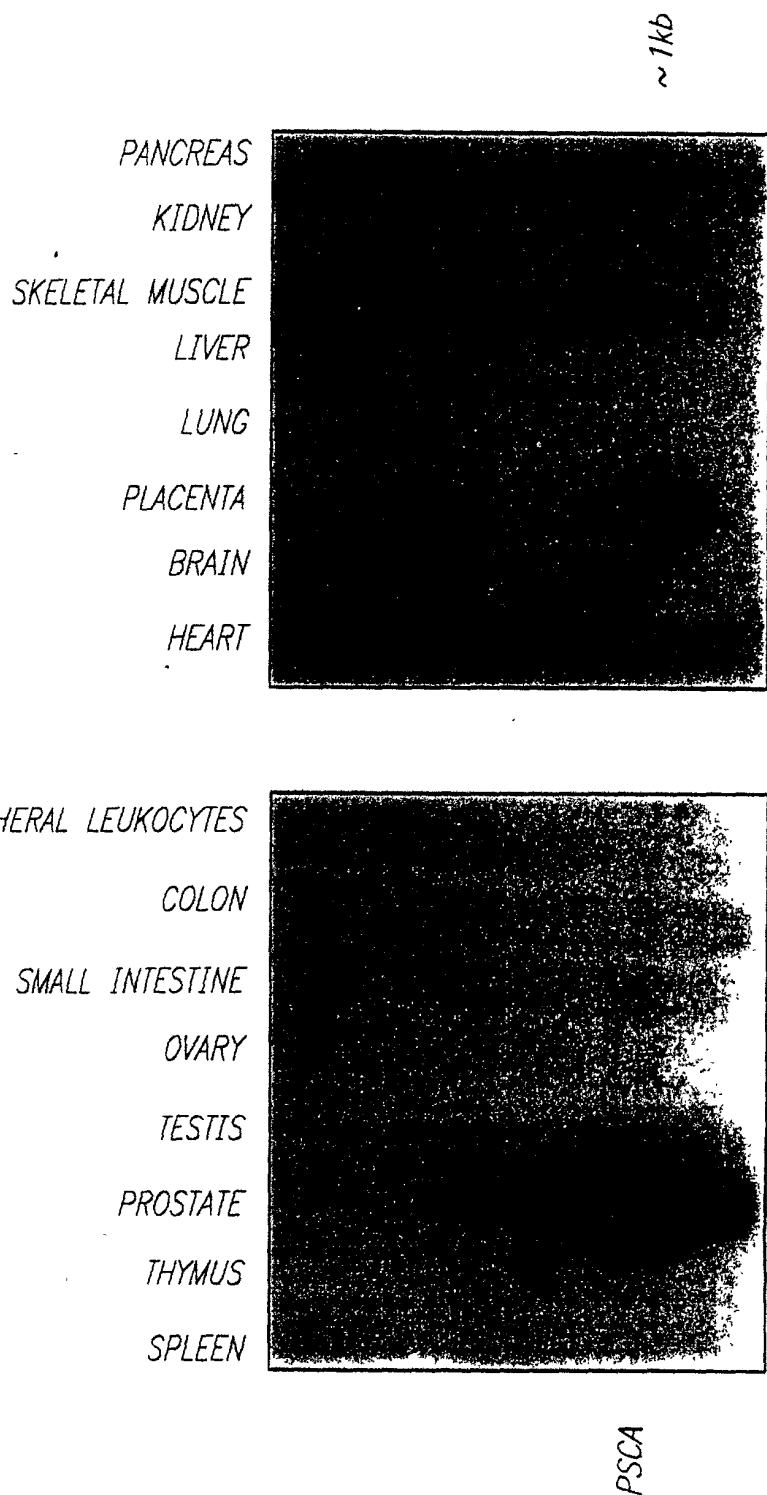


FIG. 9B

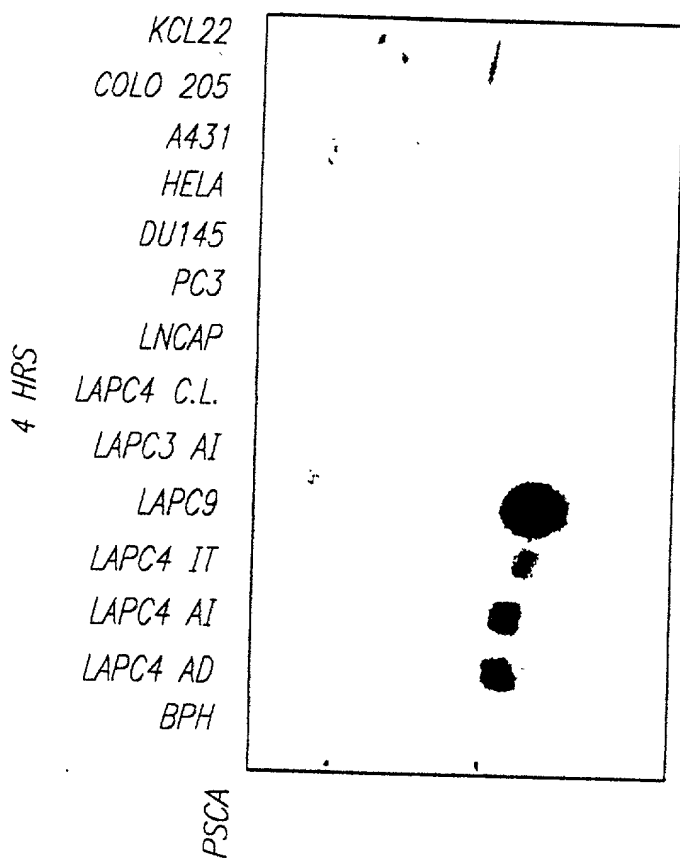
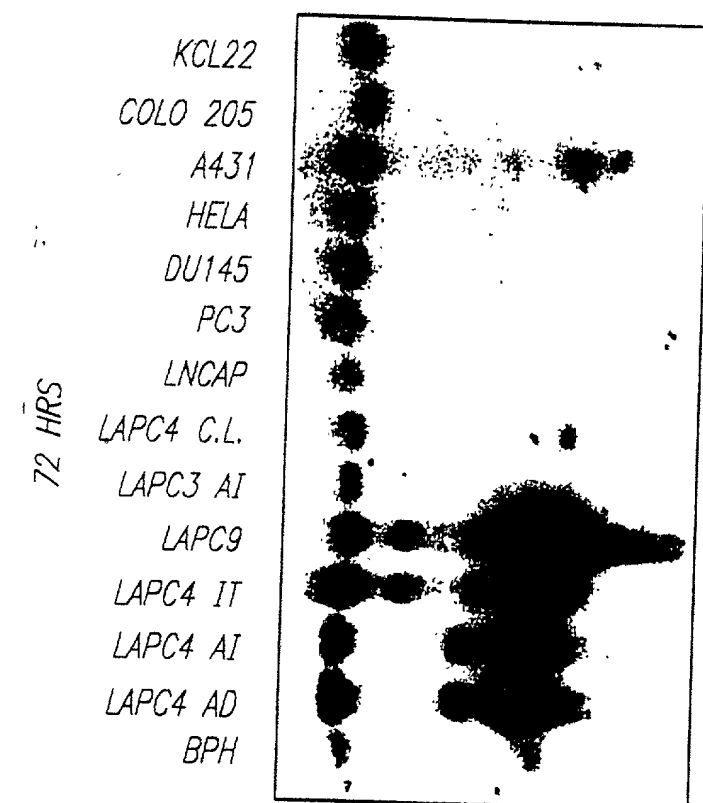


FIG. 10-1

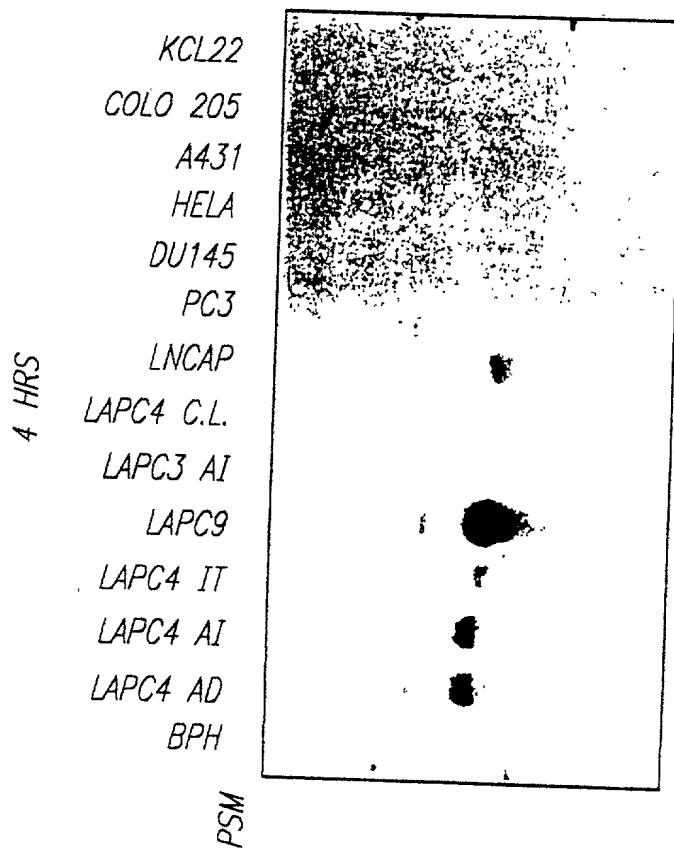
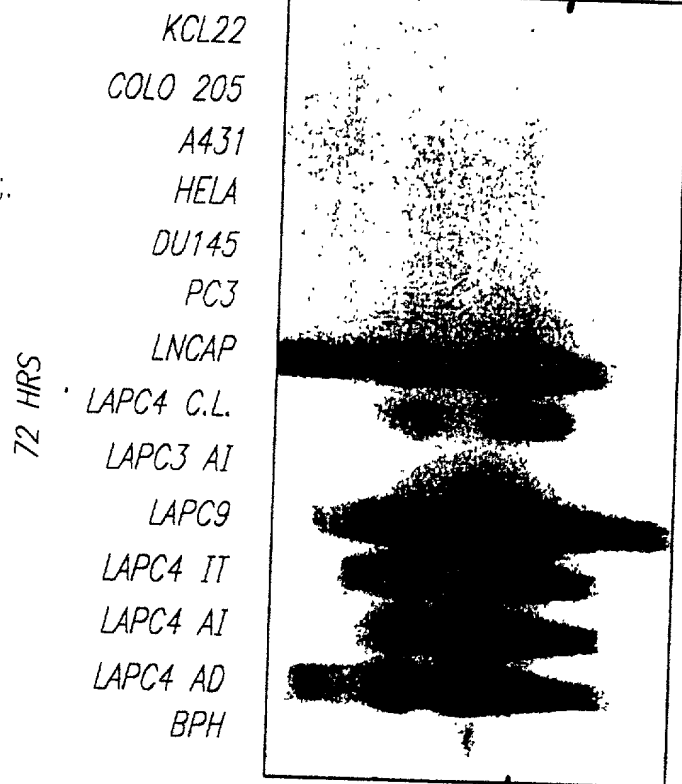


FIG. 10-2

707280 6/24/66

72 HRS

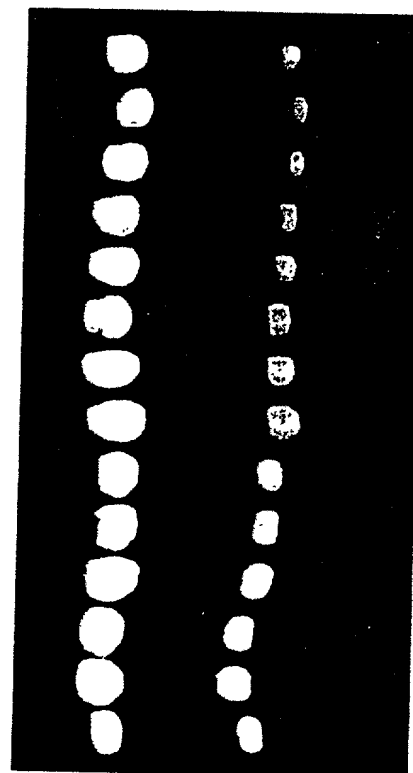
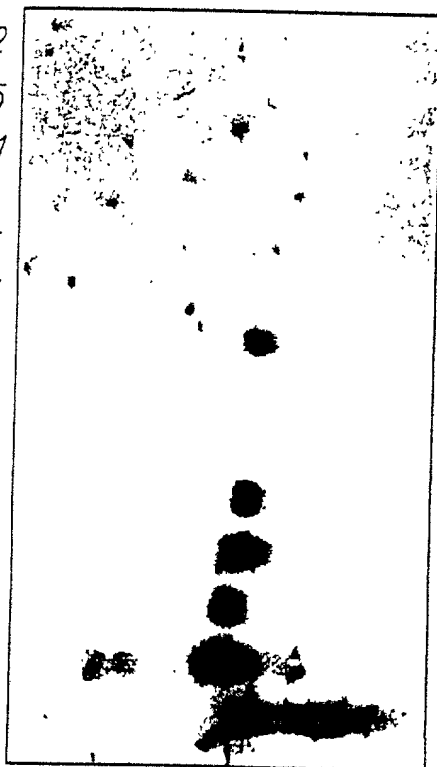
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A431
HELA
DU145
PC3
LNCAP
LAPC4 C.L.
LAPC3 AI
LAPC9
LAPC4 IT
LAPC4 AI
LAPC4 AD
BPH



4 HRS

KCL22
COLO 205
A431
HELA
DU145
PC3
LNCAP
LAPC4 C.L.
LAPC3 AI
LAPC9
LAPC4 IT
LAPC4 AI
LAPC4 AD
BPH

PSA



ETBR

FIG. 10-3

FIG. 11A



FIG. 11B

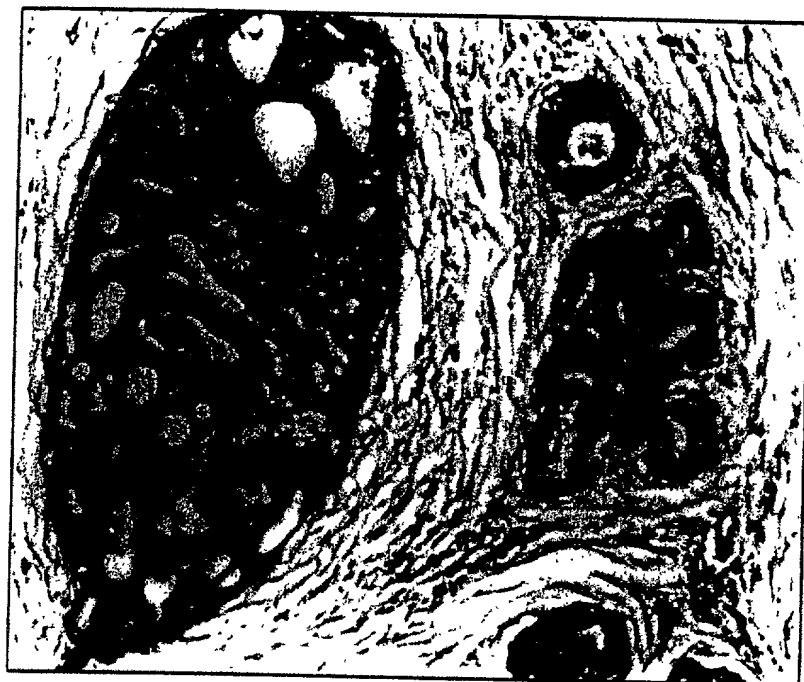
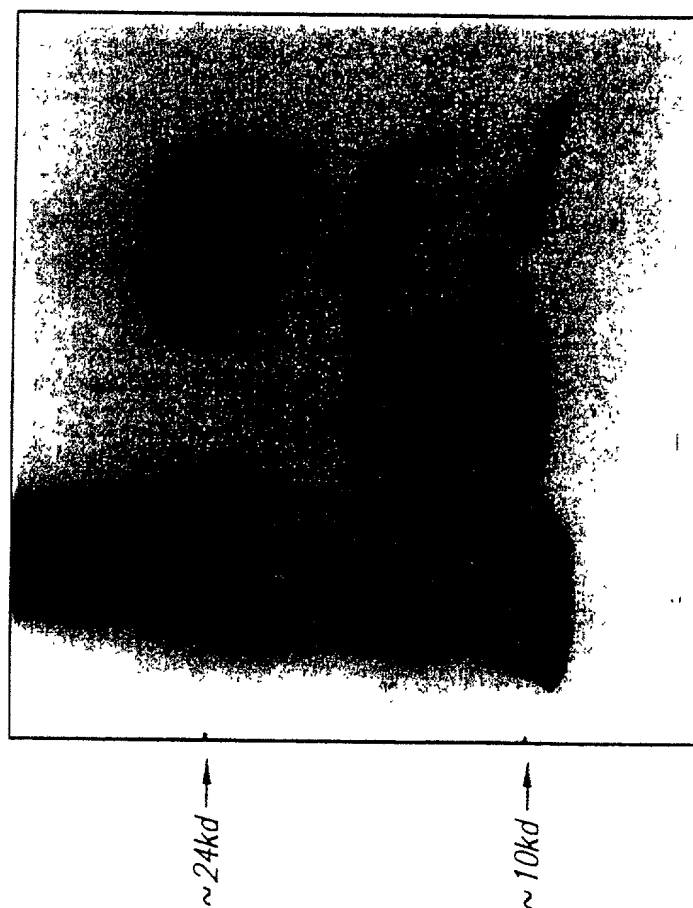


FIG. 11C

101-230 6248660

FIG. 12A

CONTROL
N GLYCOSIDASE F
O GLYCOSIDASE



CELL ASSOCIATED
SECRETED

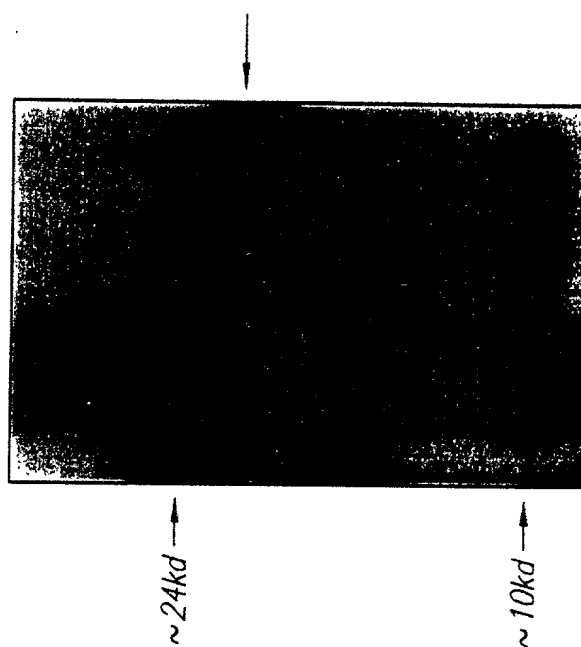


FIG. 12B

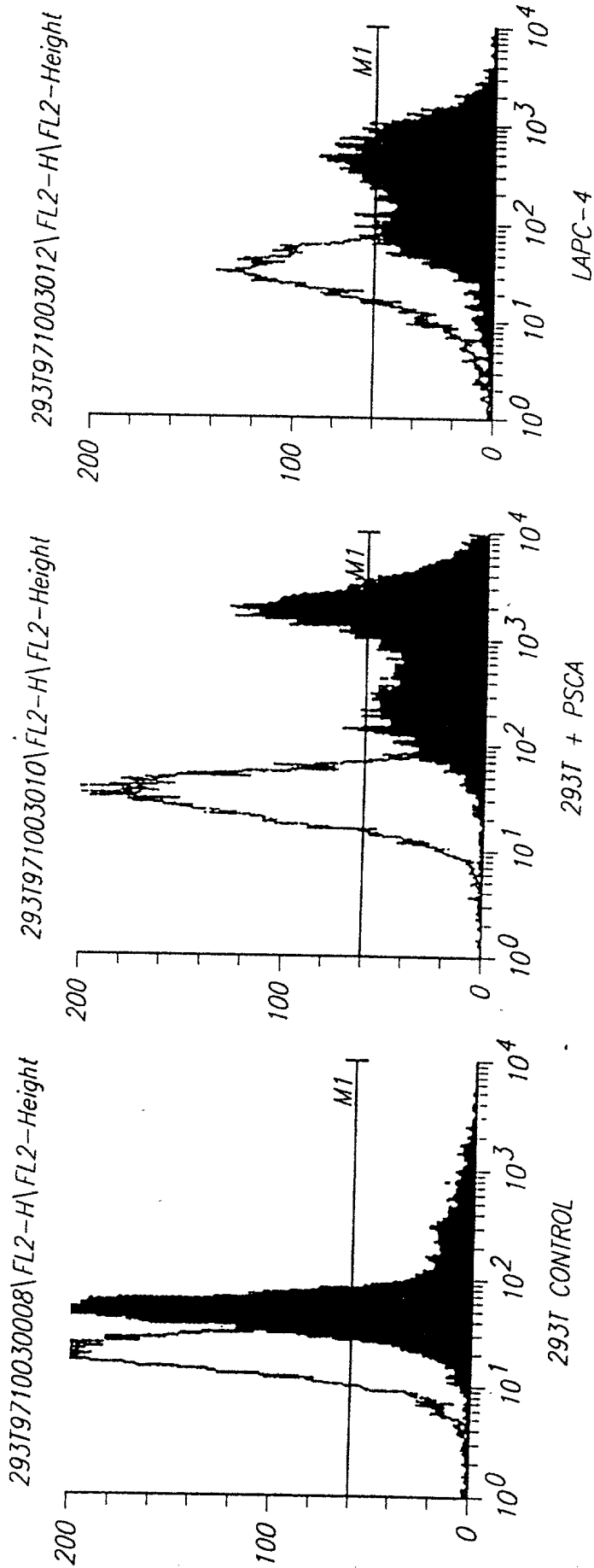


FIGURE 12C

PSCA Maps to Chromosome 8q24.2



Fluorescent
in Situ Hybridization
Analysis of PSCA

FIGURE 13

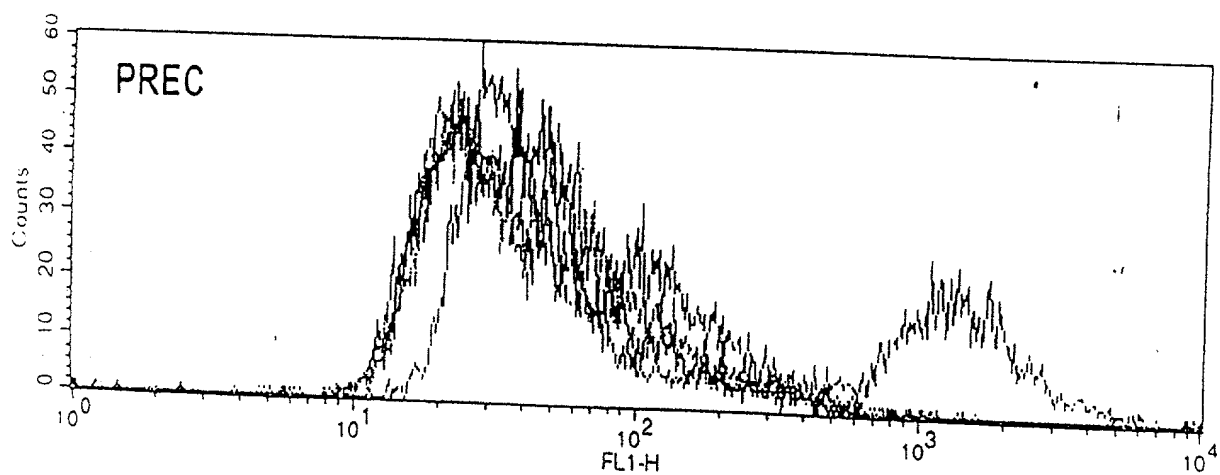
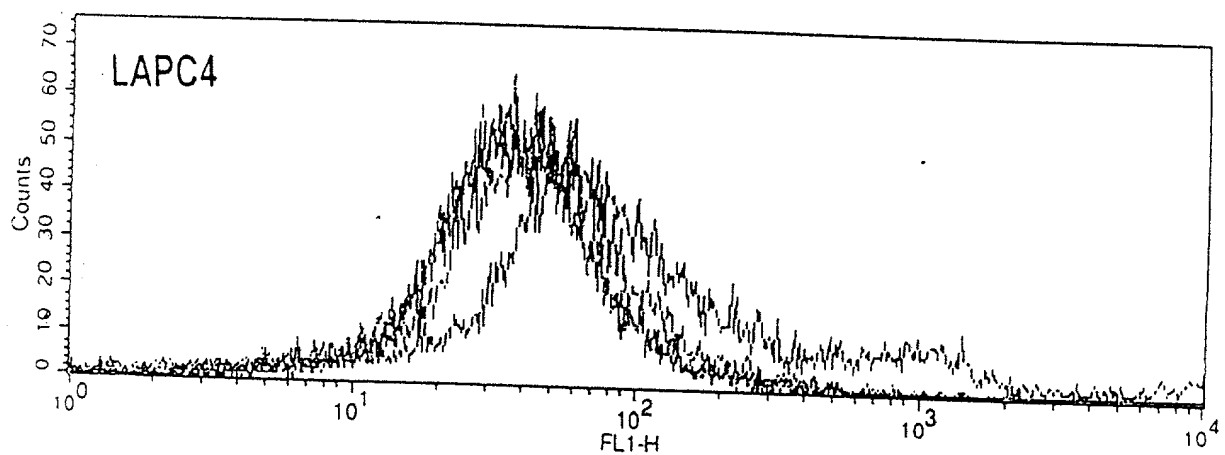
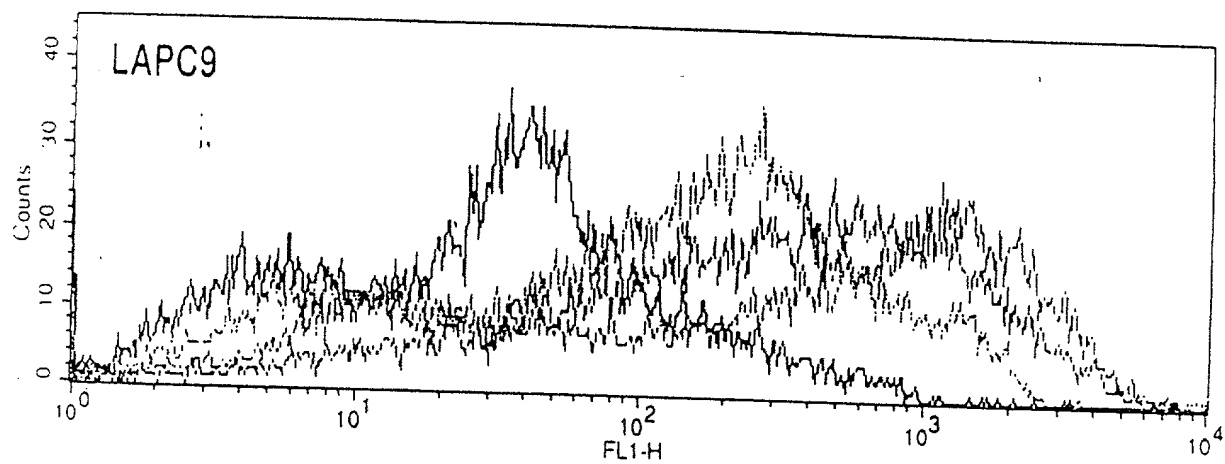


FIGURE 14

A

Epitope map

mAb	Isotype	FL (18-98)	N (2-50)	M (46-109)	C (85-123)
1G8	IgG1 k	2.039	0.007	0.628	0.000
2H9	IgG1 k	1.318	0.863	0.032	0.021
3C5	IgG2a k	2.893	1.965	0.016	0.005
3E6	IgG3 k	0.328	0.024	0.069	0.370
4A10	IgG2a k	2.039	1.315	0.000	0.014
2A2	IgG2a k	1.366	0.733	0.010	0.003
3G3	IgG2a k	2.805	1.731	0.004	0.000

B

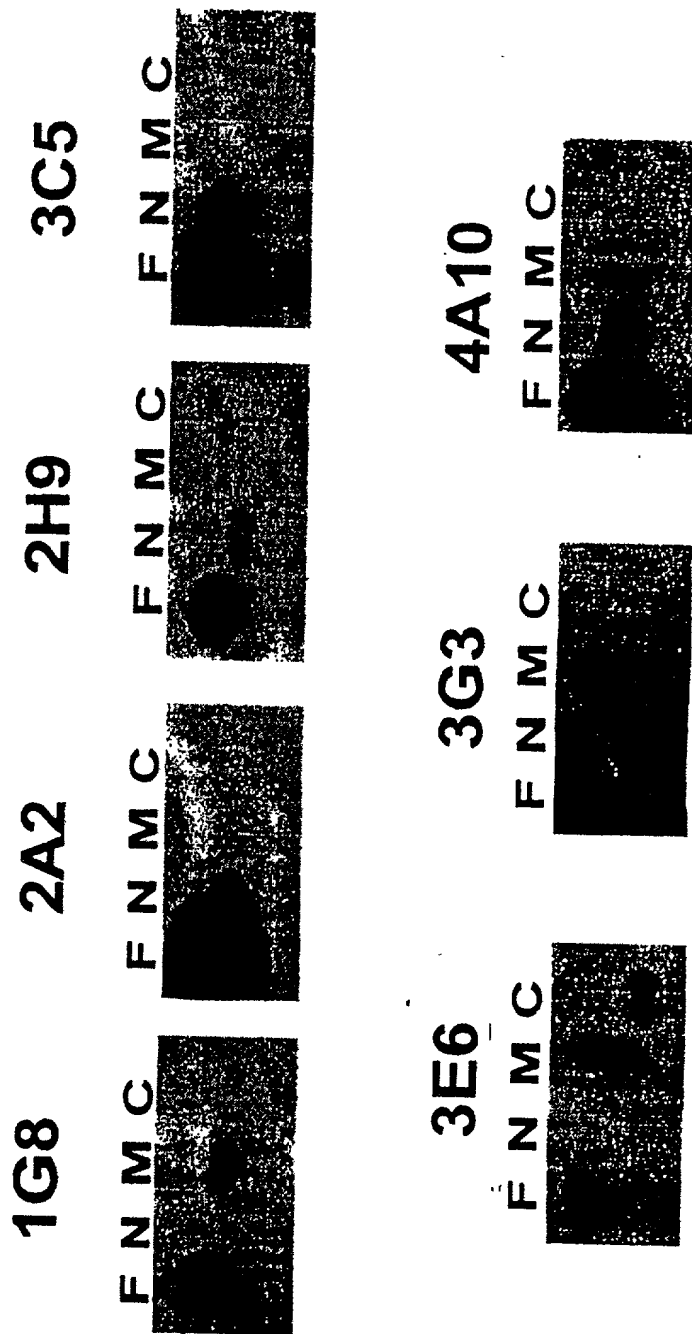


FIGURE 15

Prostate Stem Cell Antigen (PSCA) is a GPI-anchored Protein

	I	E	S	M	P	/	D	E	L	A	A	/	L	I	S	/	E	R	D		hSCA-2				
1	A	E	E	L	A	T	E	T	M	A	D	E	A	L	/	P	G	I	/	A	hPSCA				
1	T	A	E	E	L	D	E	A	T	/	L	A	L	/	P	G	/	A		mPSCA					
21	M	C	E	S	C	/	L	/	Q	/	S	N	*	L	/	C	L	/							
21	L	C	E	S	C	/	K	/	A	/	S	N	*	E	/	D	C	L	/	V	N*				
21	L	C	E	S	C	/	K	/	A	/	S	N	*	P	/	D	C	L	/	N	V	N*			
41	C	S	/				C	/	T	/	A	S	A	/											
41	C	S	/				C	/	T	/	R	I	R	/	A	/	G	L	/	T					
41	C	S	/				C	/	T	/	R	I	R	/	A	/	G	L	/	T					
61	V	/					S	/	K	/	C	S	/	A	/	C	/								
61	V	/					I	/	S	/	K	/	G	/	C	S	/	D	/	C	D	D	S		
61	V	/					I	/	S	/	K	/	G	/	C	S	/	D	/	C	D	D	S		
81	V	N	/	D	/	A	S	/	M	/	S	/	I	/	C	C	/	S	/	F	L	C	N	*	
76	D	/	V	/	G	/	K	/	N	/	E	/	T	/	C	/	C	/	T	/	D	L	C	N	*
76	N	/	L	/	G	/	K	/	N	/	E	/	T	/	C	/	C	/	T	/	D	L	C	N	*
101	S	A	/	D	/	G	/	C	/	R	/	A	/												
95	S	A	/	D	/	G	/	C	/	R	/	A	/												
95	N	/	L	/	G	/	K	/	N	/	E	/	T	/	C	/	C	/	T	/	D	L	C	N	*
121	S	/	P	/	A	/	L	/	E	/	R	/													
115	S	/	P	/	A	/	L	/	E	/	R	/													
115	S	/	P	/	A	/	L	/	E	/	R	/													

(Reiter, R.E., et al., 1997, *PNAS*)

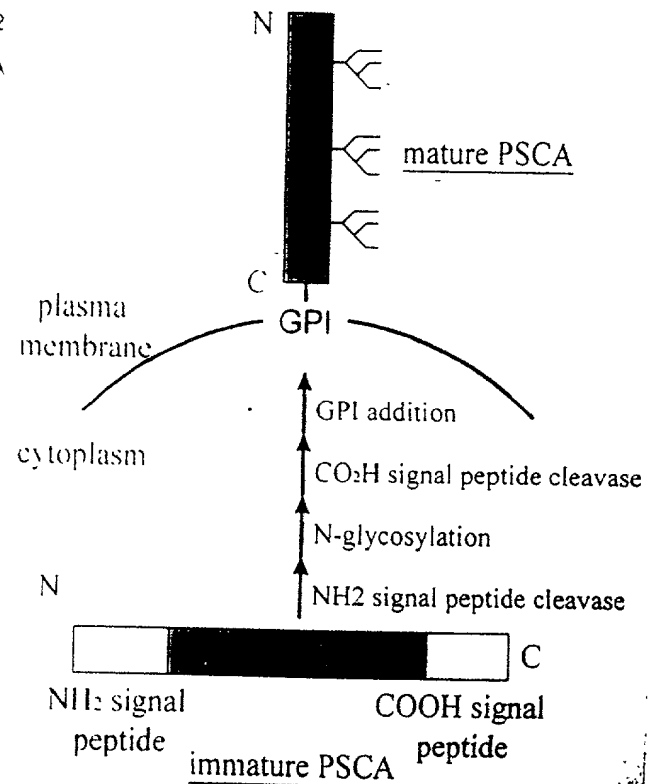
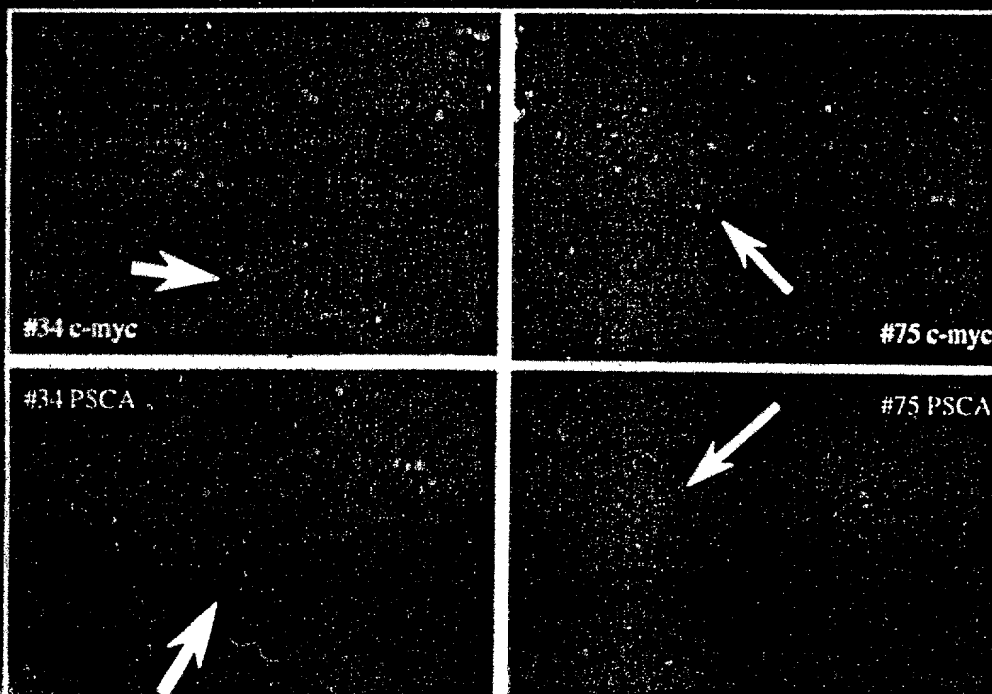


FIGURE 16

FISH Analysis of PSCA and c-myc in Prostate Cancer

Gain Chromosome 8

Amplification



R. Jenkins

FIGURE 17

10/23/00 6/2/44550

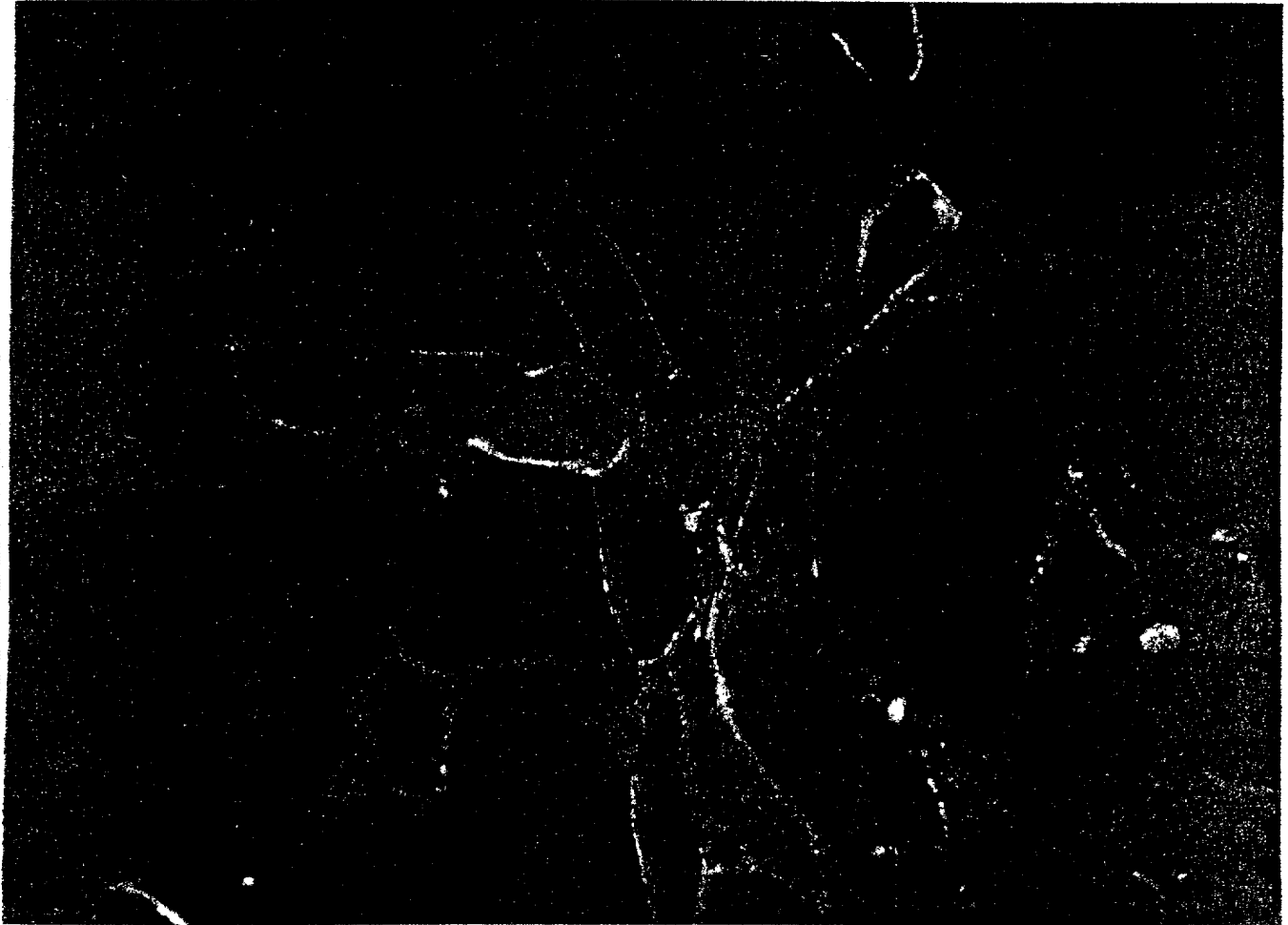


FIGURE 18

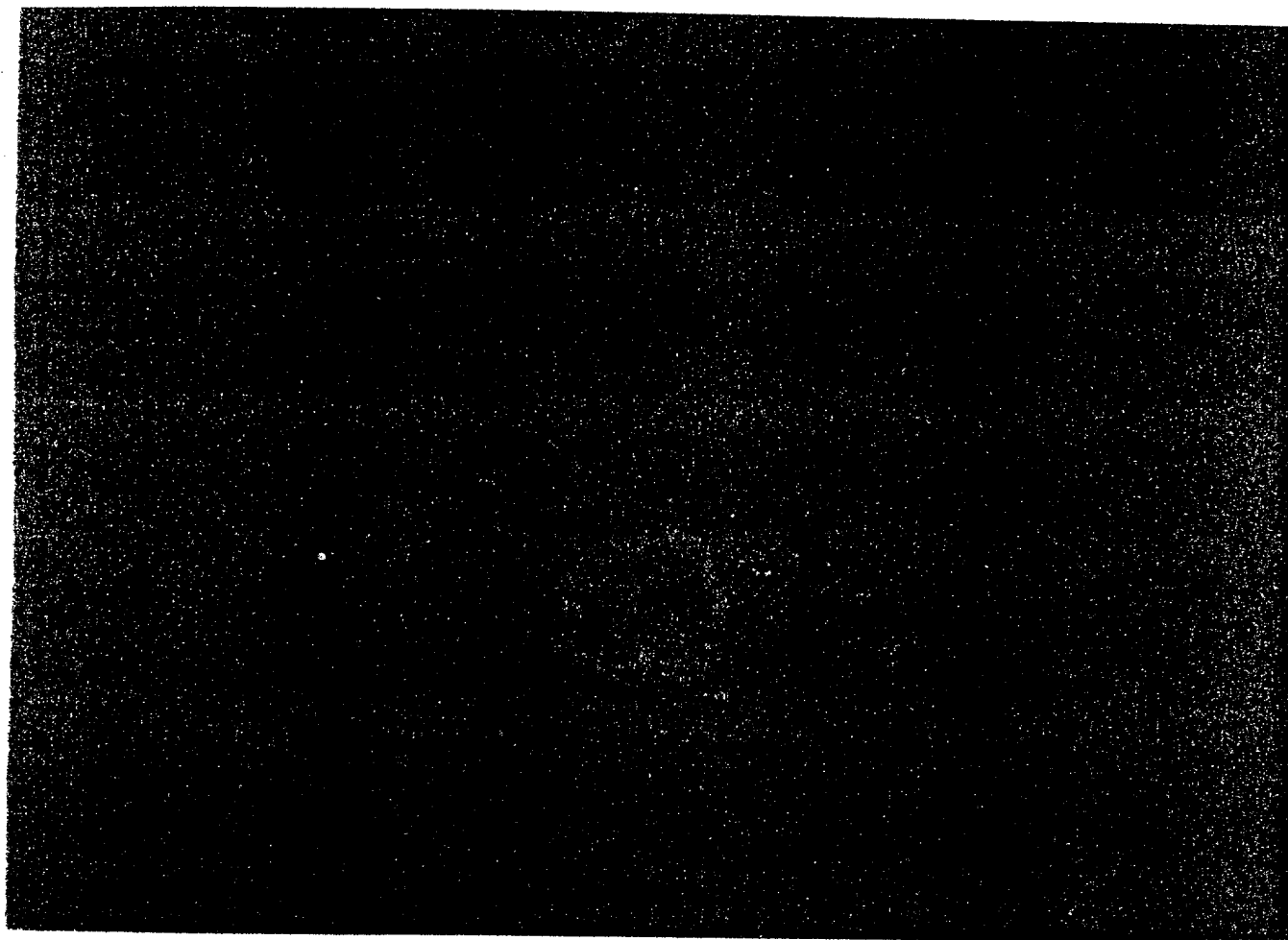


FIGURE 20

PSCA Immunostaining of Primary Tumors

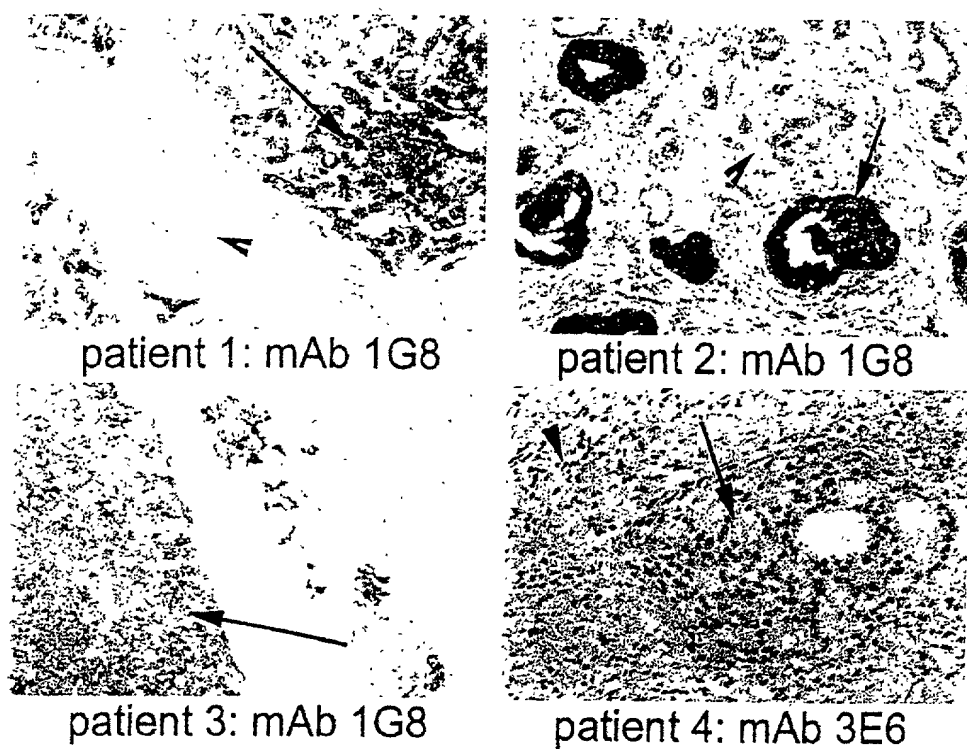


FIGURE 21

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FIGURE 22

407330 6/4/66



FIGURE 23

09547 09550 09553 09556 09559 09562 09565 09568 09571 09574 09577 09580 09583 09586 09589 09592 09595 09598 09601 09604 09607 09610 09613 09616 09619 09622 09625 09628 09631 09634 09637 09640 09643 09646 09649 09652 09655 09658 09661 09664 09667 09670 09673 09676 09679 09682 09685 09688 09691 09694 09697 09700 09703 09706 09709 09712 09715 09718 09721 09724 09727 09730 09733 09736 09739 09742 09745 09748 09751 09754 09757 09760 09763 09766 09769 09772 09775 09778 09781 09784 09787 09790 09793 09796 09799 09802 09805 09808 09811 09814 09817 09820 09823 09826 09829 09832 09835 09838 09841 09844 09847 09850 09853 09856 09859 09862 09865 09868 09871 09874 09877 09880 09883 09886 09889 09892 09895 09898 09901 09904 09907 09910 09913 09916 09919 09922 09925 09928 09931 09934 09937 09940 09943 09946 09949 09952 09955 09958 09961 09964 09967 09970 09973 09976 09979 09982 09985 09988 09991 09994 09997

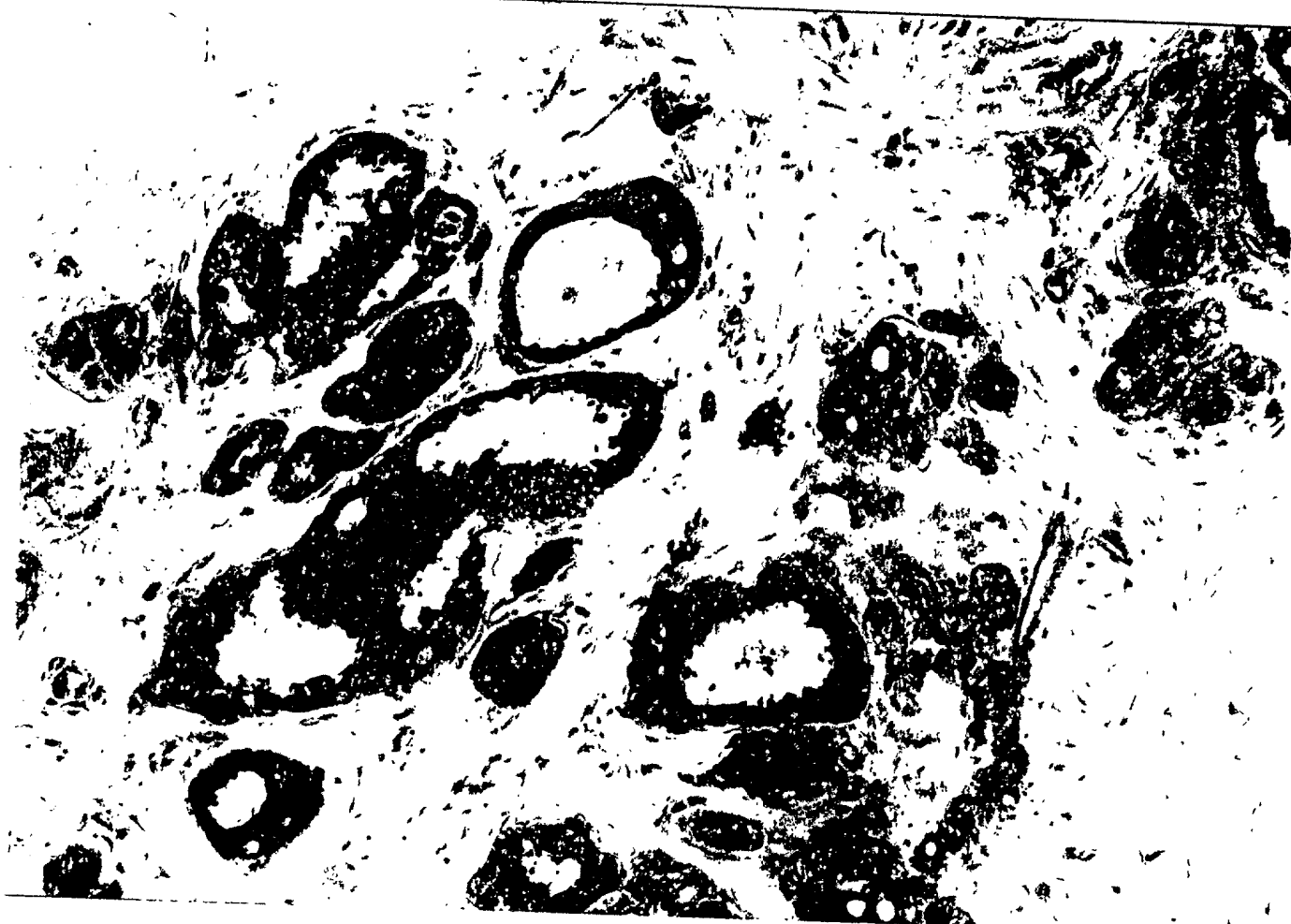


FIGURE 24

[Faint handwritten notes at bottom left]

FIGURE 25

401-224 6/24/50

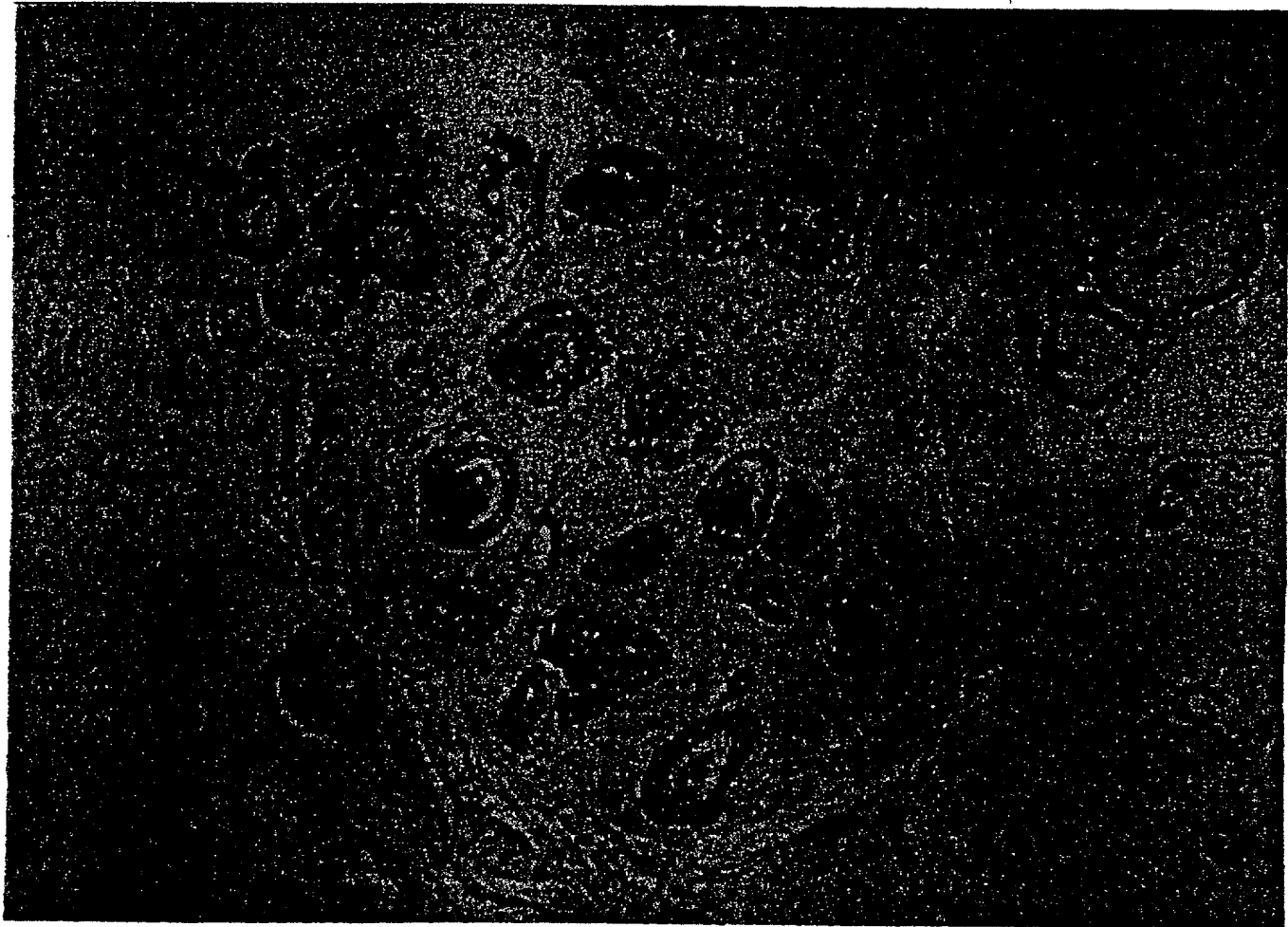


FIGURE 26

A high-contrast, black and white photograph of a large, irregularly shaped, light-colored object, possibly a piece of debris or a biological specimen, resting on a dark, textured surface. The object has a rough, porous appearance with many small holes and indentations. The background is dark and grainy.

FIGURE 27

PSCA Immunostaining of Bony Metastases



Patient 5: H and E
and mAb 1G8



Patient 4: H and E
and mAb 3E6

FIGURE 28

This is a high-contrast, black and white image, possibly a scan of a book cover or endpaper. The image is characterized by a dense, grainy texture with a mottled appearance. A dark, irregular shape, which could be a stain or a piece of tape, is visible in the center-right area. The overall image is very dark, with the texture being the primary visual element.

FIGURE 29

A high-contrast, black and white photograph showing a close-up of a rough, textured surface, possibly a rock or concrete. The surface is covered in numerous small, light-colored spots and patches, creating a mottled appearance. The lighting is harsh, casting deep shadows and bright highlights.

FIGURE 30

A high-contrast, black and white photograph showing a dense, textured surface, possibly a rock face or a wall. The image is characterized by a multitude of small, light-colored spots and patches, creating a speckled or mottled appearance against a dark background. The texture is irregular and granular, with some areas appearing more solid and others more eroded or pitted. The lighting is harsh, emphasizing the physical details of the surface.

FIGURE 31

This is a high-contrast, black and white image of a textured surface, likely a book cover or endpaper. The texture is dense and irregular, with a prominent vertical crease or fold line running down the center. The image is characterized by a stark contrast between deep blacks and bright whites, creating a grainy, almost abstract appearance. The lighting is uneven, with brighter areas on the left side and darker areas on the right, emphasizing the three-dimensional quality of the texture.

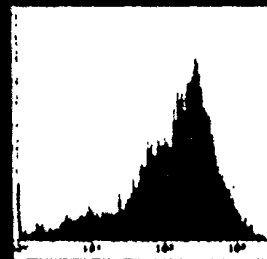
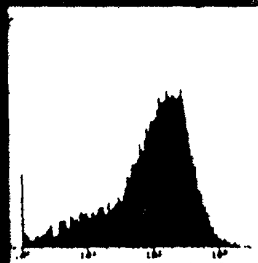
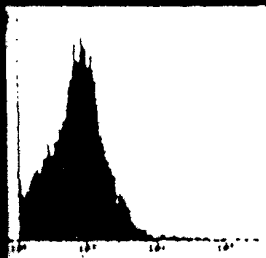
FIGURE 32

PSCA Expression in LAPC-9 Xenograft by FACS

Secondary Antibody

1G8

2H9



4A10

3C5

3E6

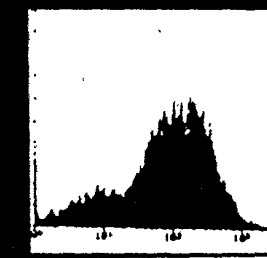
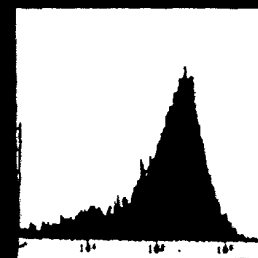
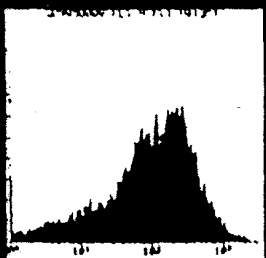


FIGURE 33

anti-PSCA mAbs



FIGURE 34

Immunofluorescent Staining of LNCaP-PSCA Cells

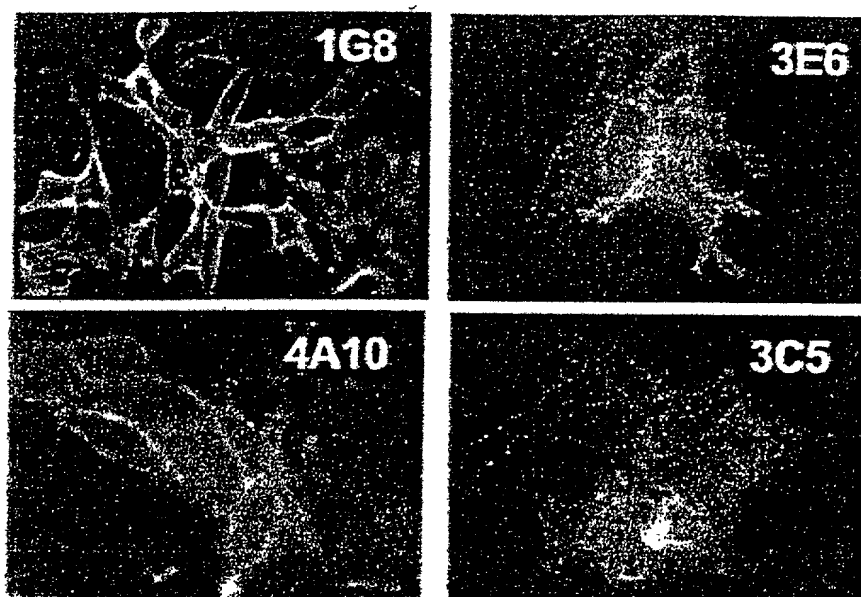


FIGURE 35

[illegible]

FIGURE 36

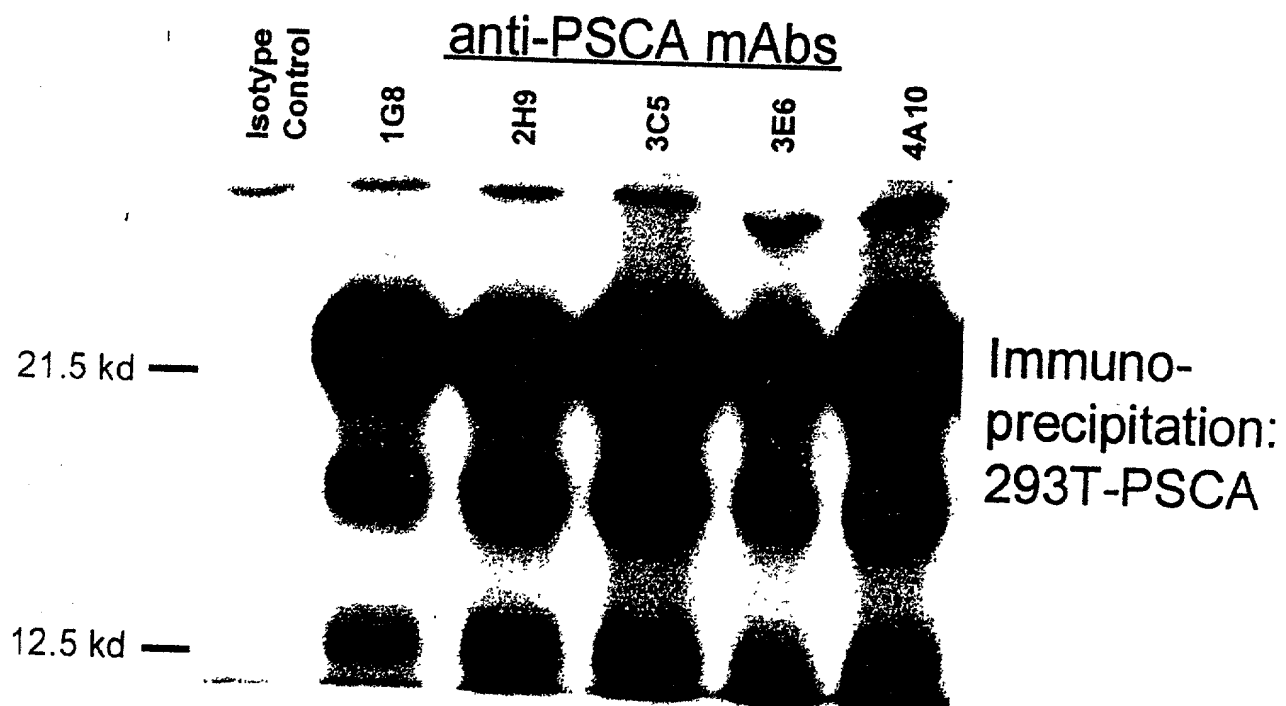


FIGURE 37

Immunohistochemical Staining of Normal Prostate

Normal: Isotype Control



Normal: PSCA mAb 3E6



Normal: PSCA mAb 1G8



Atrophy: PSCA mAb 2H9



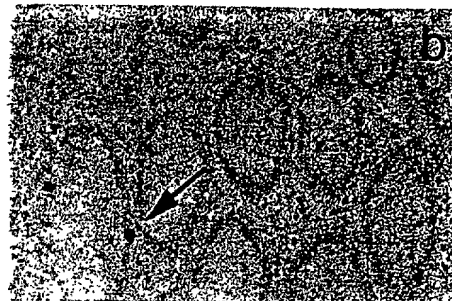
FIGURE 38

1.07280 E/24E660

A.



Bladder: 1G8



Colon: 1G8



Kidney: 3E6



Placenta: 3E6

B.

Prostate
Prostate
Prostate
Kidney
Kidney
Kidney
Bladder
Bladder
Bladder
LAPC 9

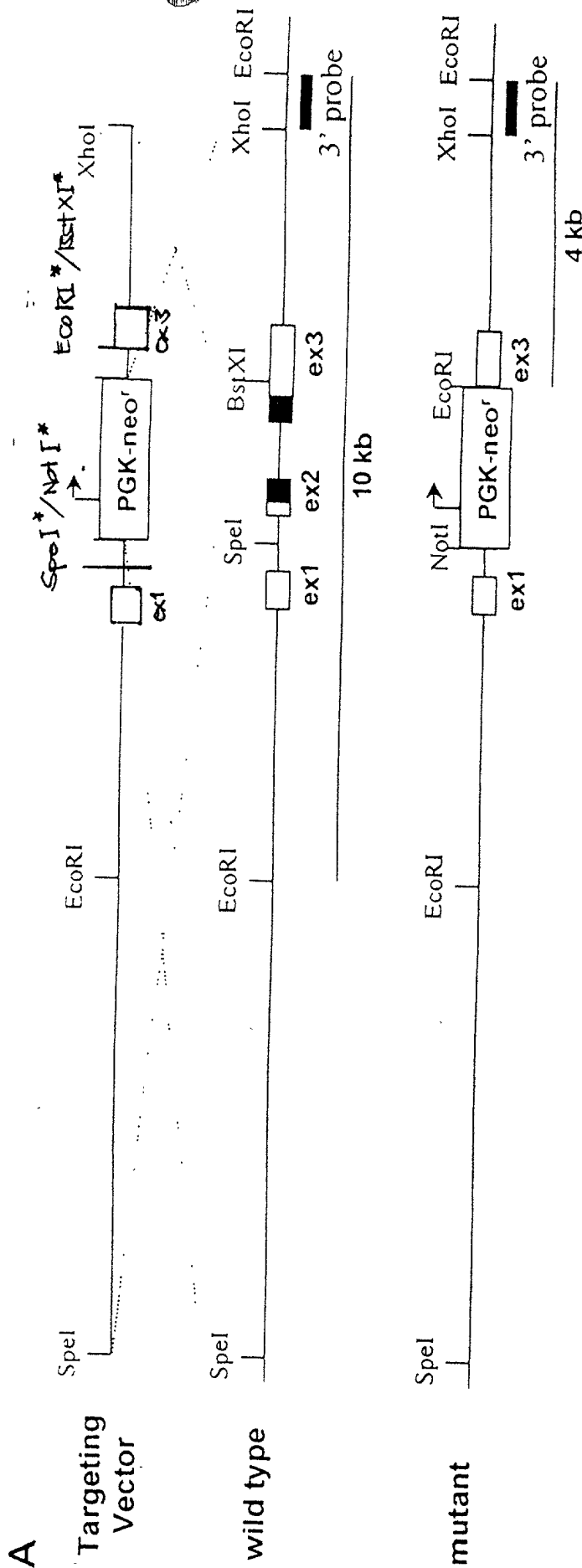


PSCA

Actin

FIGURE 39

Targeting of Mouse PSCA Gene



B. Genomic Southern Analysis of ES Cells

* ex1, 2, and 3 are the exons of PSCA gene.
 * Black boxes of ex2 and ex3 encode PSCA mature protein sequences.
 * ES genomic DNA's were digested with EcoRI, followed by Southern hybridization using 3' probe.

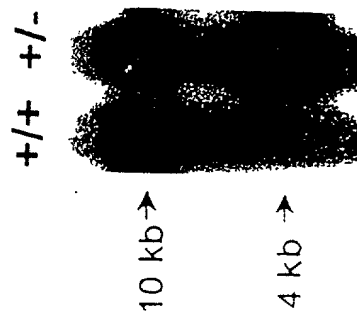
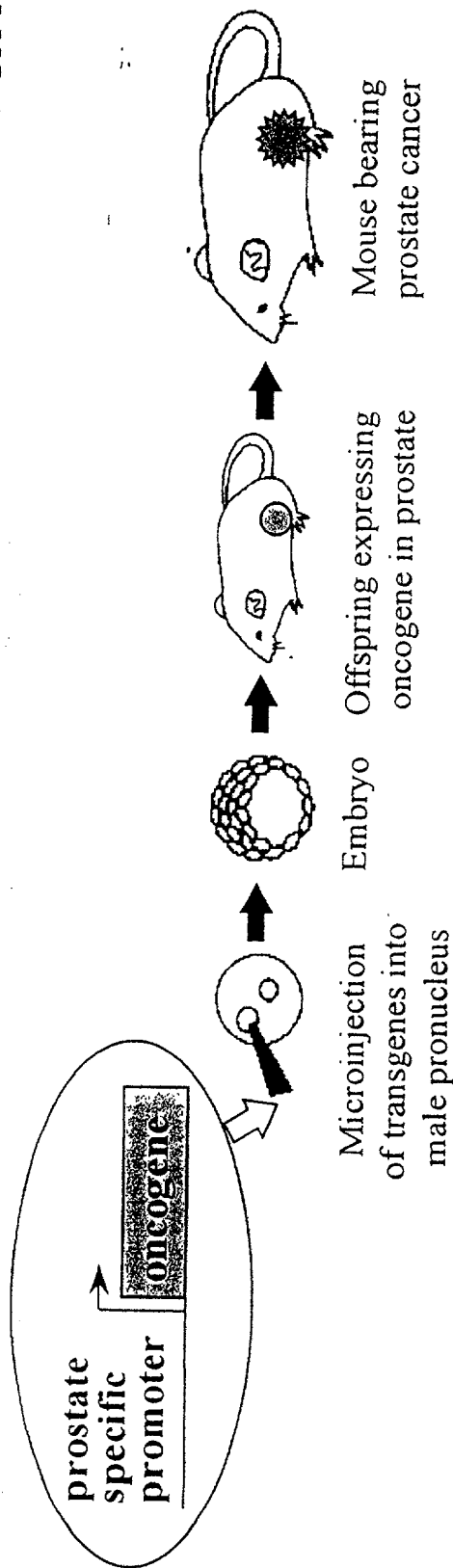


FIGURE 40

Transgenic Mouse Models of Prostate Cancer



Transgene	Target tissues	Characteristics
C3(1) (-3 kb)/ SV40 large+small T <i>Maroulakou et al.</i> 1994 <i>PNAS</i>	prostate (secretory cells) urethral, mammary and sweat gland	Low-grade PIN 8-12 wks High-grade PIN 8-12 wks Invasive carcinoma 28 wks No metastases
Probasin (-426 bp)/ SV40 large+small T <i>Greenberg et al.</i> 1995 <i>PNAS</i>	prostate (secretory cells)	Low-grade PIN 5-8 wks High-grade PIN 8-12 wks Invasive carcinoma 12 wks Metastases in lymph node, lung, liver and bone
Cryptdin2 (-6.5 kb)/ SV40 large+small T <i>Garabedian et al.</i> 1998 <i>PNAS</i>	prostate (neuroendocrine cells) small intestine	Low-grade PIN 8-12 wks High-grade PIN 8-12 wks Invasive carcinoma 16 wks Metastases in lymph node, lung, liver and bone

FIGURE 41

Reporter Gene Constructs for Transfection Assay

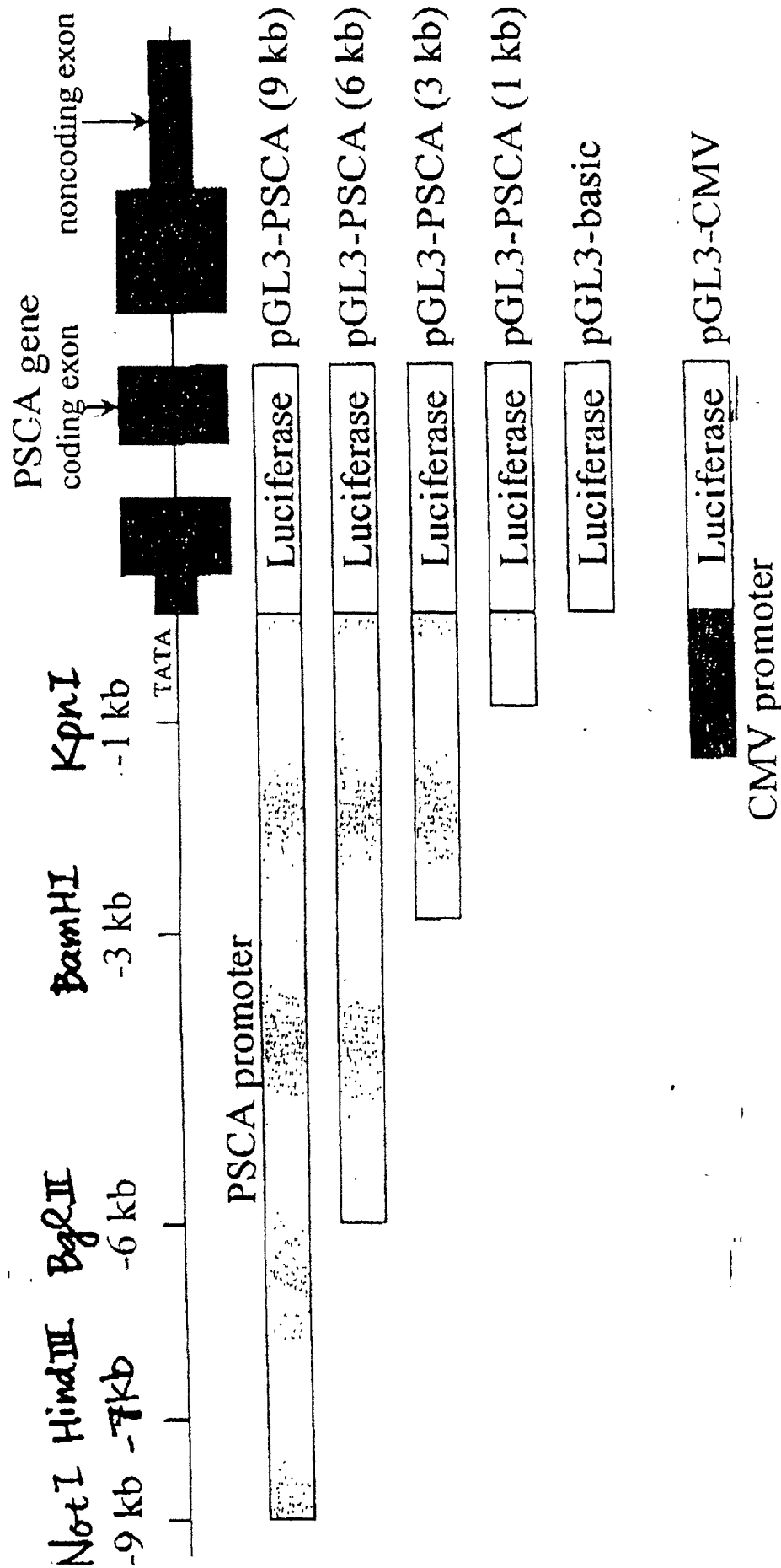


FIGURE 42

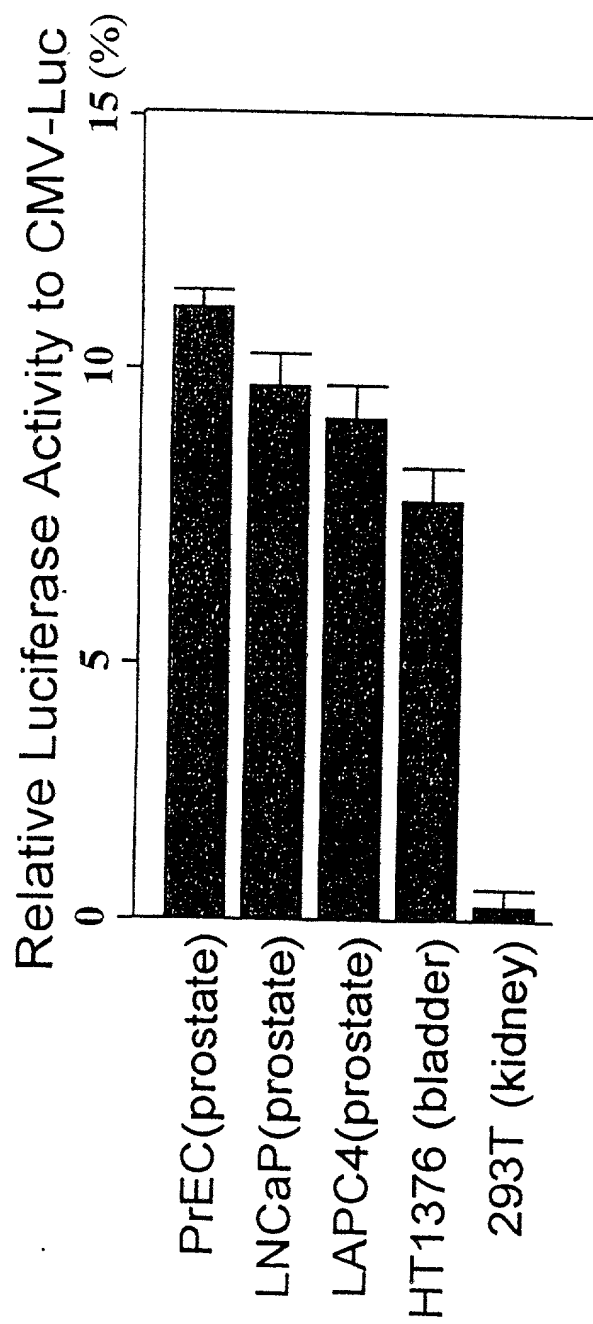


FIGURE 43

Identification of Prostate-Specific Elements Within PSCA Promoter Sequences

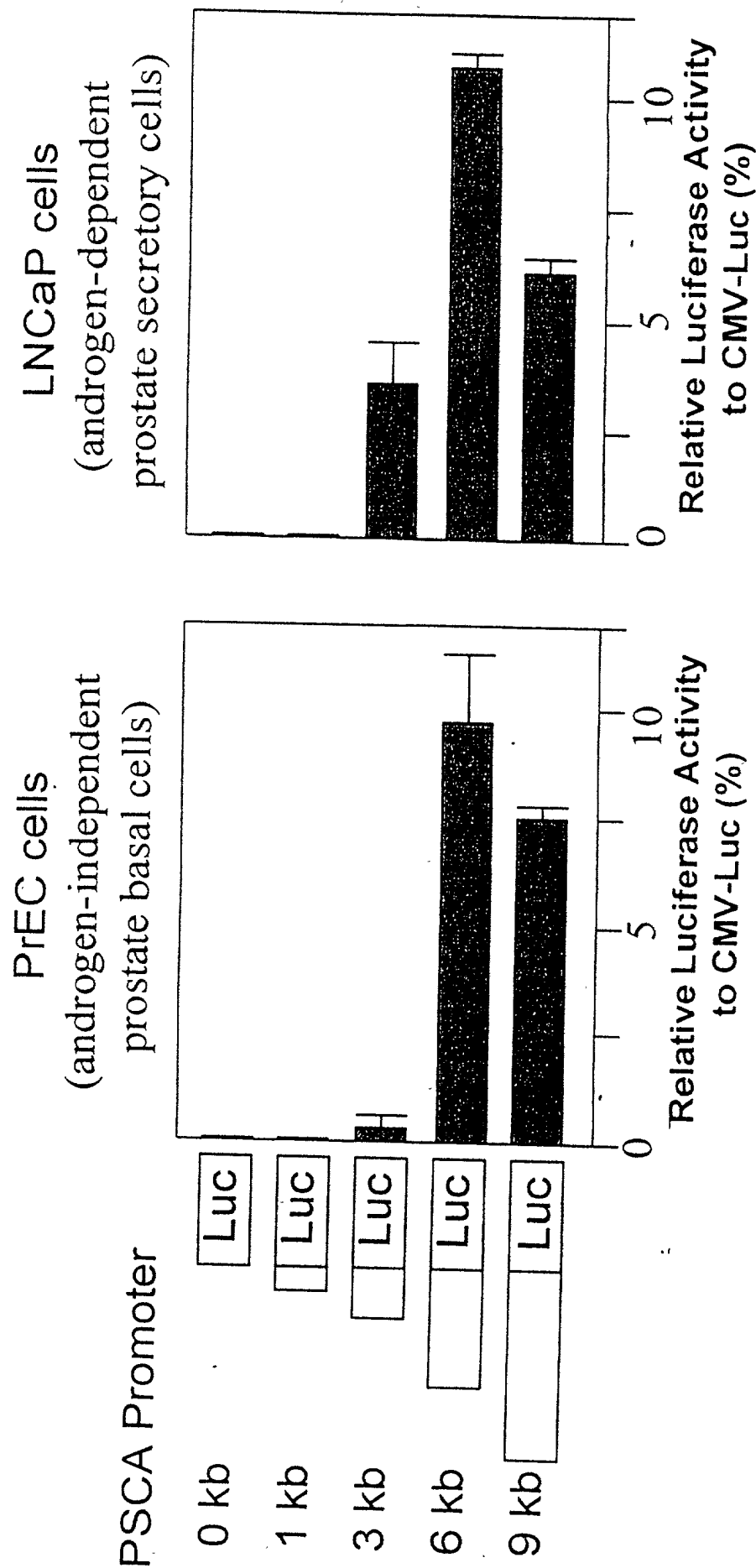


FIGURE 44

Update of Transgenic Mouse Projects

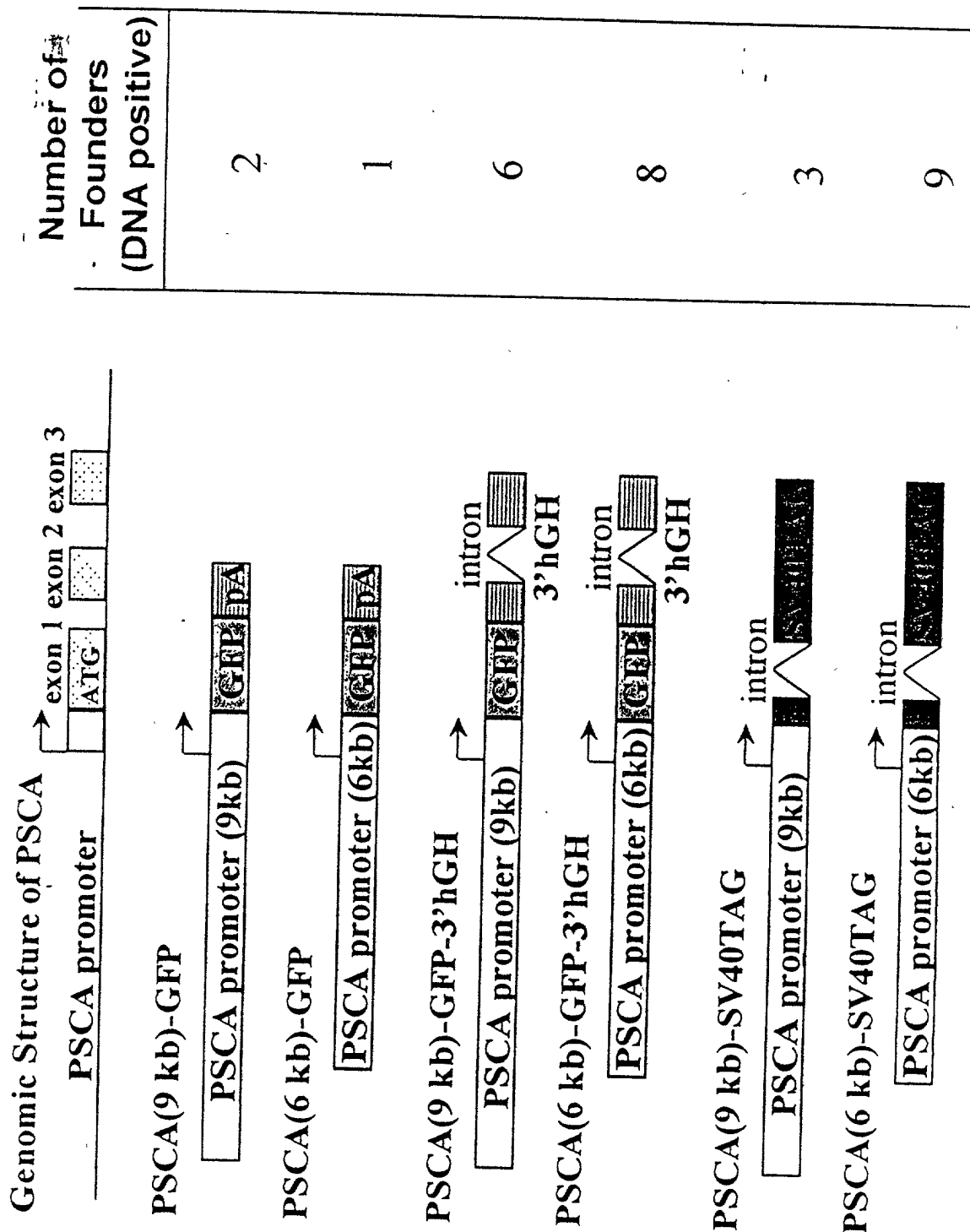
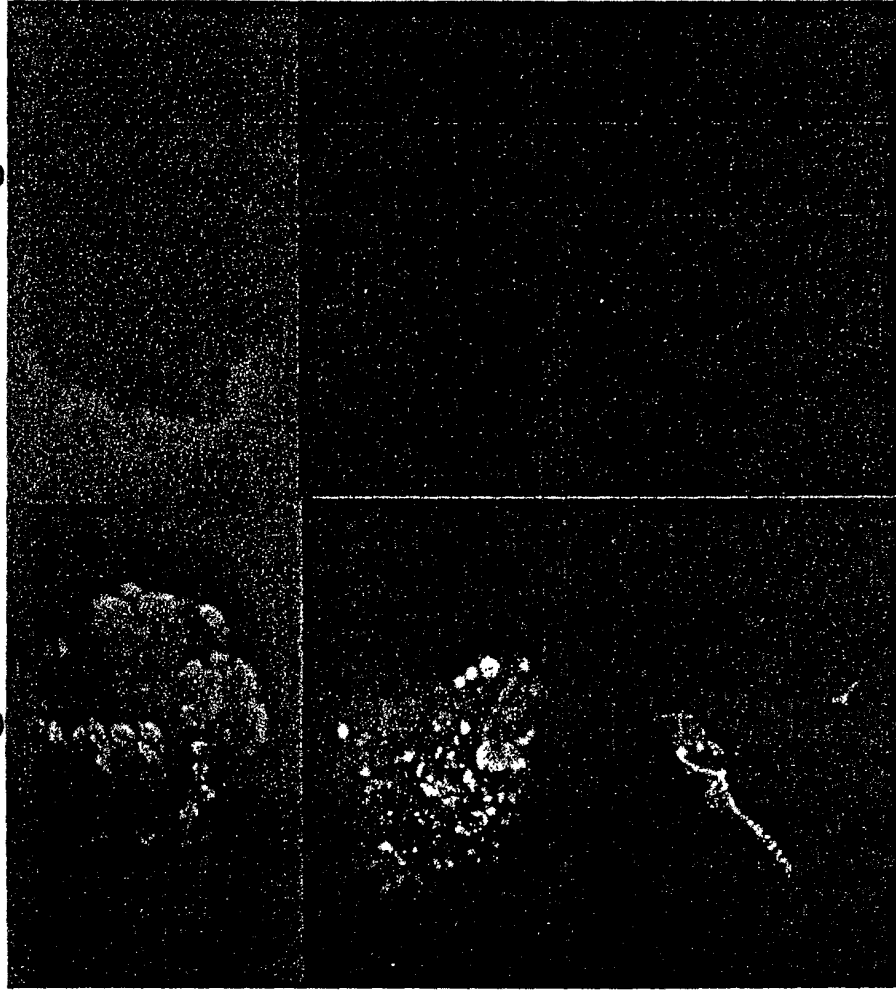


FIGURE 45

Negative tissues

Stomach
 Small intestine
 Colon
 Seminal Vesicle
 Urethra
 Testis
 Liver
 Kidney
 Lung
 Brain
 Heart
 Skeletal muscle
 Ovary
 Uterus

Whole-mount green fluorescence image
 Transgenic Non-transgenic



Prostate
 (A25-106-2)

Bladder
 (A25-104)

Skin
 (A25-106-2)

HUMAN

Spleen
Thymus
Prostate
Testis
Ovary
S. int.
Colon
PBL

Spleen
Thymus
Prostate
Testis

Probus

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Northern Analysis

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Ventral prostate
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Seminal vesicle
Urethra
Testis
Kidney

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10/10/2010

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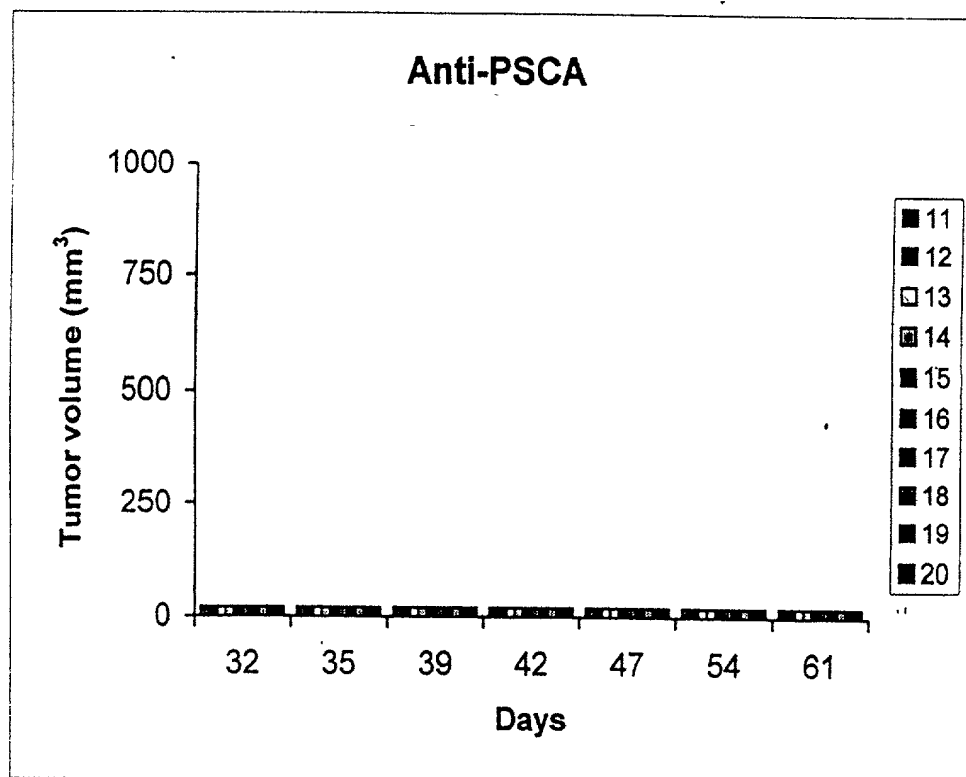
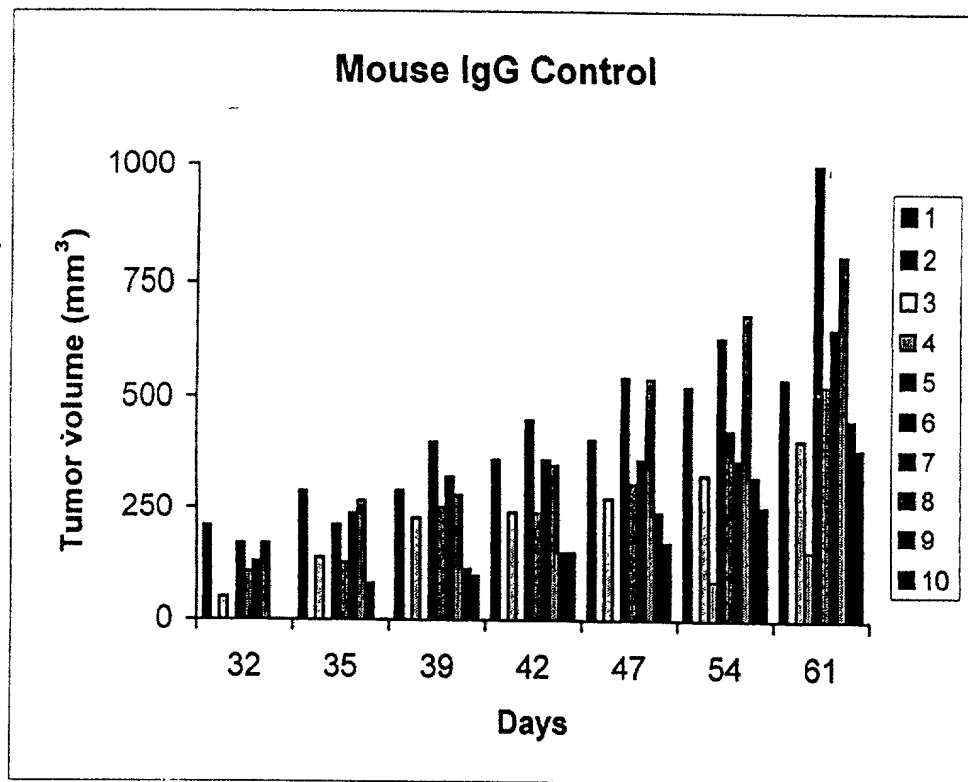
Small image of a person's face, partially obscured by a large, stylized, abstract graphic element.

mPSCA →

mG3PDH \uparrow

RT-PCR

FIGURE 47

[illegible]

A

FIG. 49

Epitope recognized (OD 450 nm)

<u>mAb</u>	<u>Isotype</u>	<u>F (18-98)</u>	<u>N (2-50)</u>	<u>M (46-109)</u>	<u>C (85-123)</u>
1G8	IgG1 k	1.485	0.004	1.273	0.003
2A2	IgG2a k	0.973	0.631	0.023	0.010
2H9	IgG1 k	1.069	1.026	0.002	0.001
3C5	IgG2a k	1.916	1.709	0.006	0.002
3E6	IgG3 k	1.609	0.036	1.133	2.118
3G3	IgG2a k	2.805	1.731	0.004	0.000
4A10	IgG2a k	1.053	0.493	0.000	0.001

B

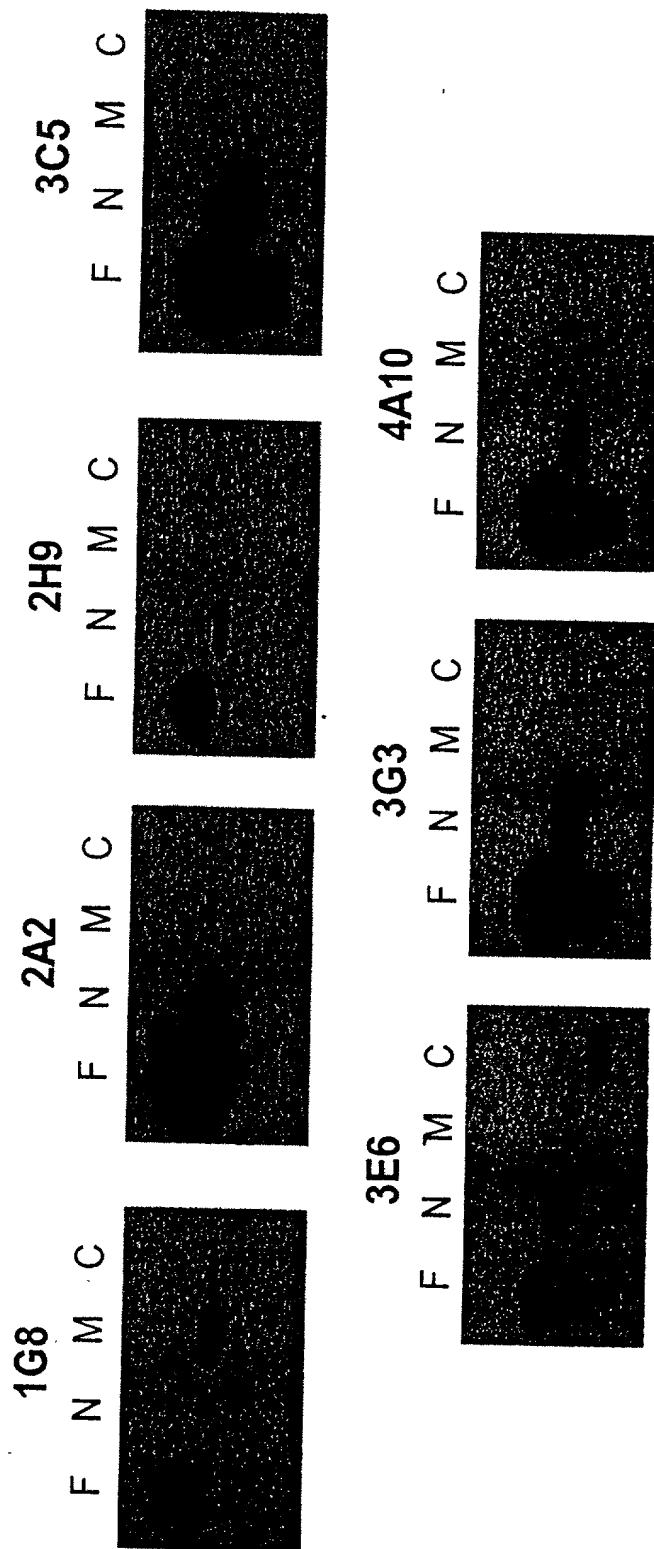
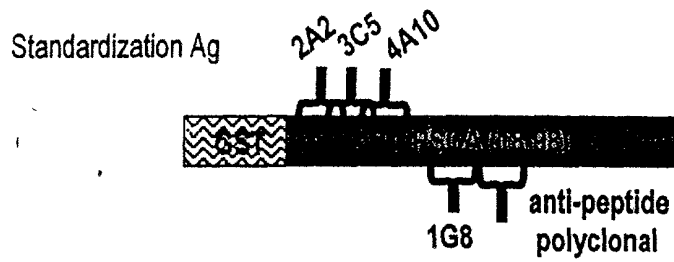
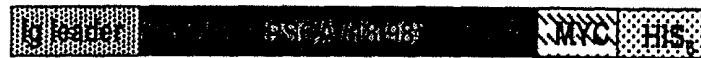


FIG. 50

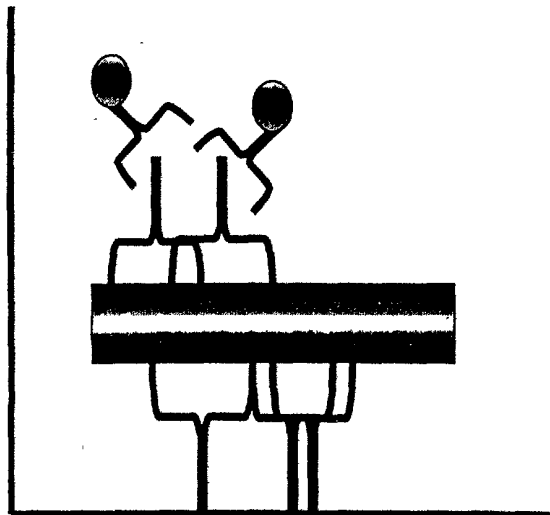
A



Engineered mammalian secreted form



B



Anti-IgG2a HRP

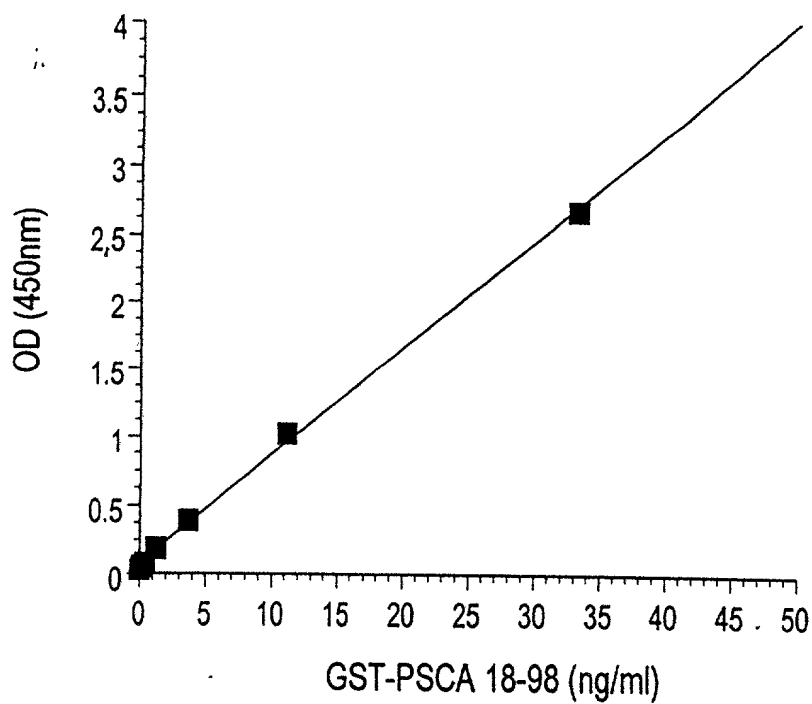
Anti-PSCA mAbs 3C5+4A10+2A2 (IgG2a)

PSCA

Affinity purified anti-peptide polyclonal
+ mAb 1G8 (IgG1)

FIG. 51

A



B

<u>Sample</u>	<u>OD+range (n=2)</u>	<u>ng/ml</u>
vector	0.005+0.001	ND
vector+hu serum	0.004+0.001	ND
secPSCA	2.695+0.031	32.92
secPSCA+hu serum	2.187+0.029	26.55

FIG. 52

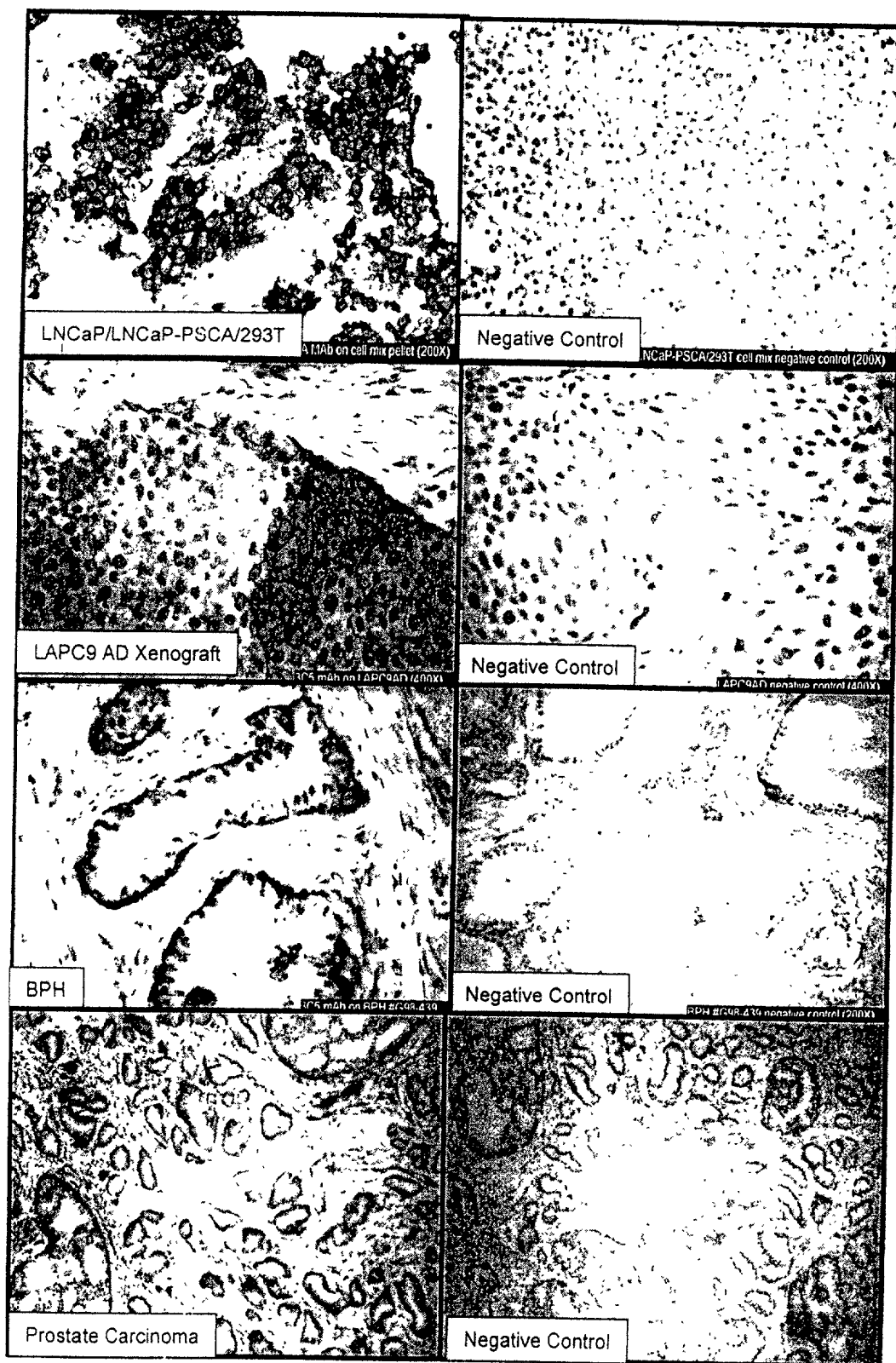


FIG. 53

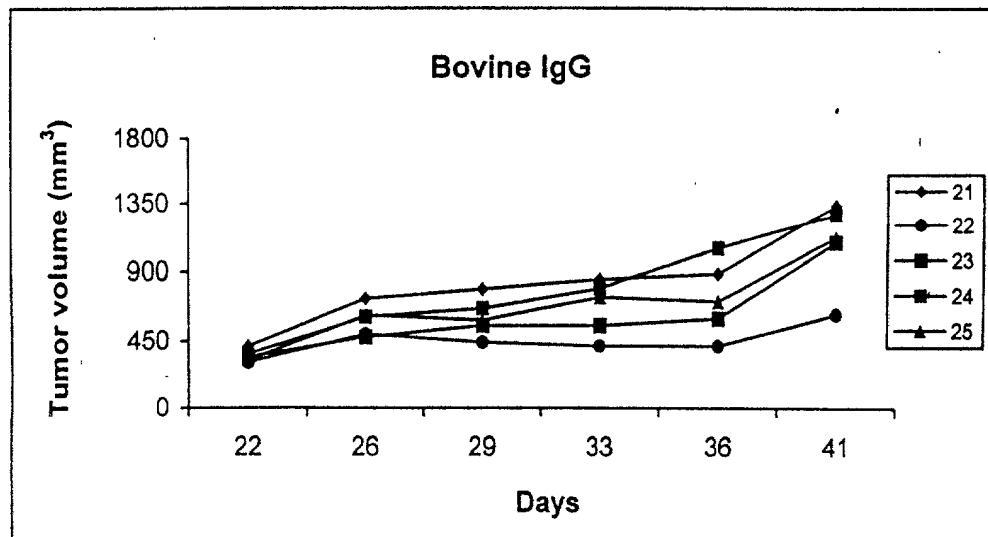
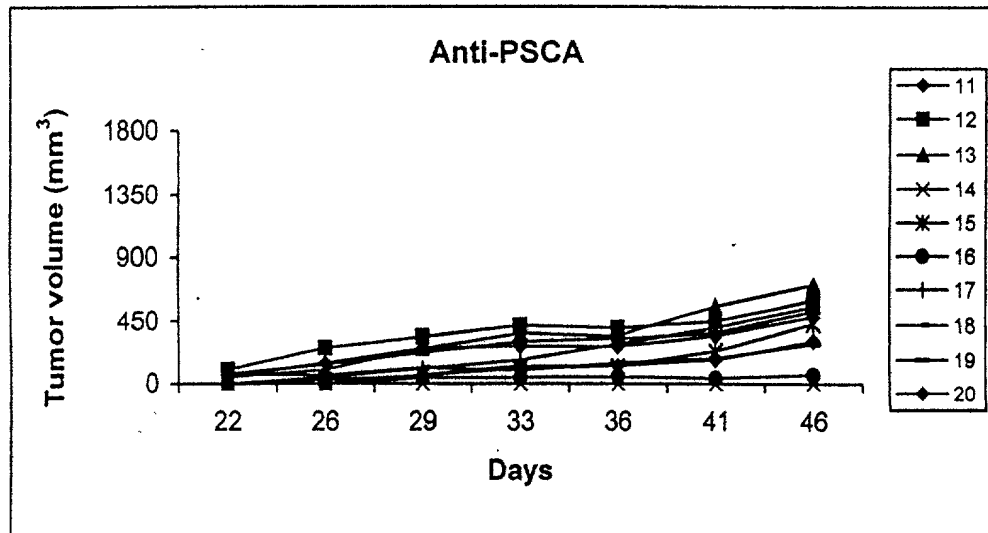
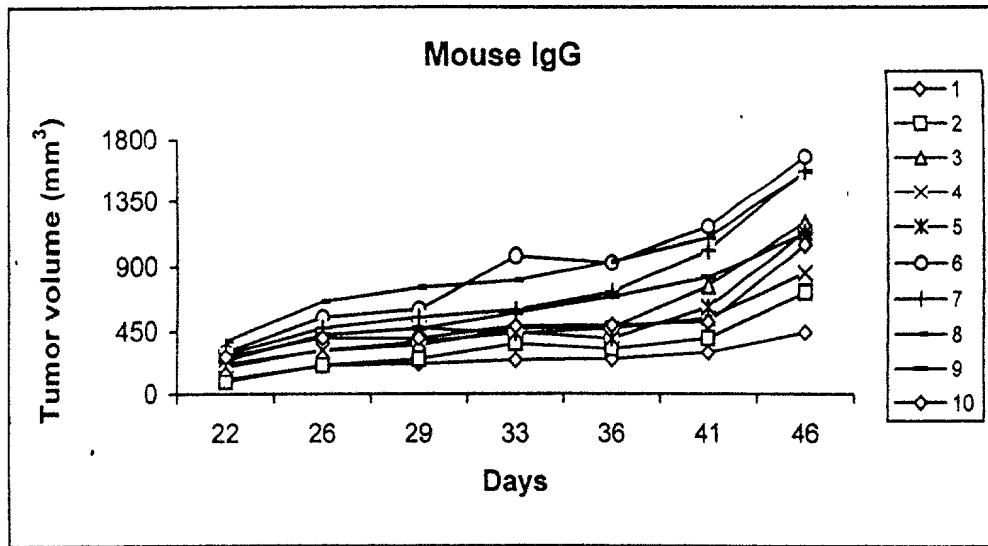


FIG. 54

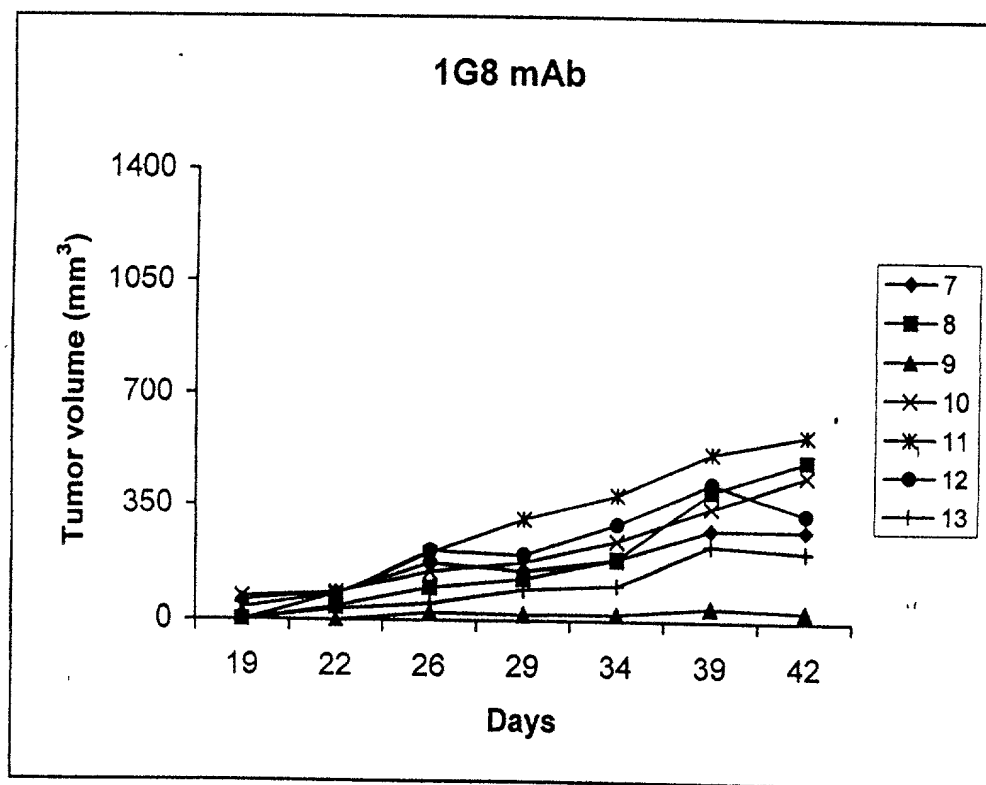
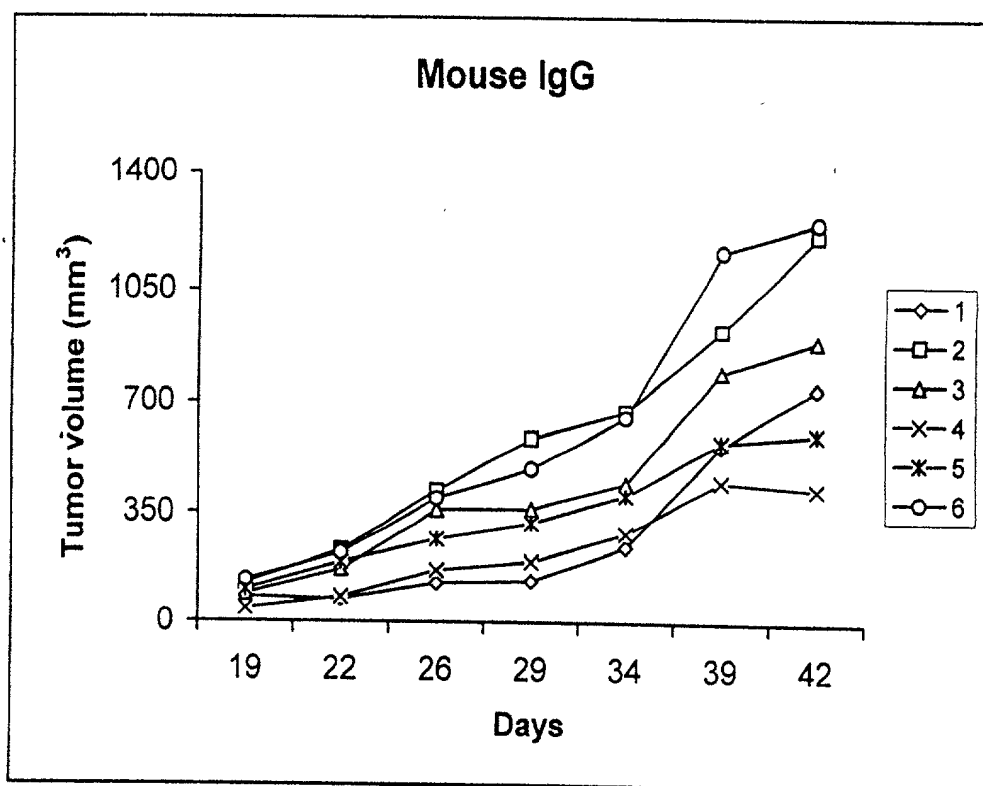


FIG. 55

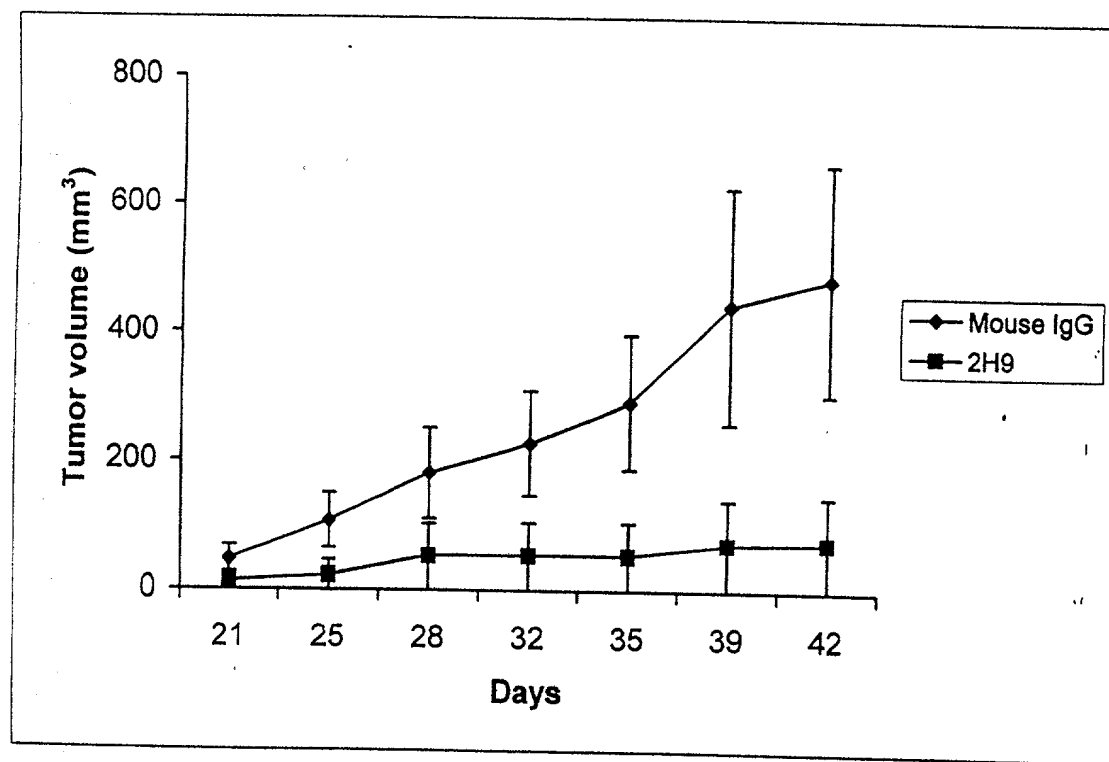
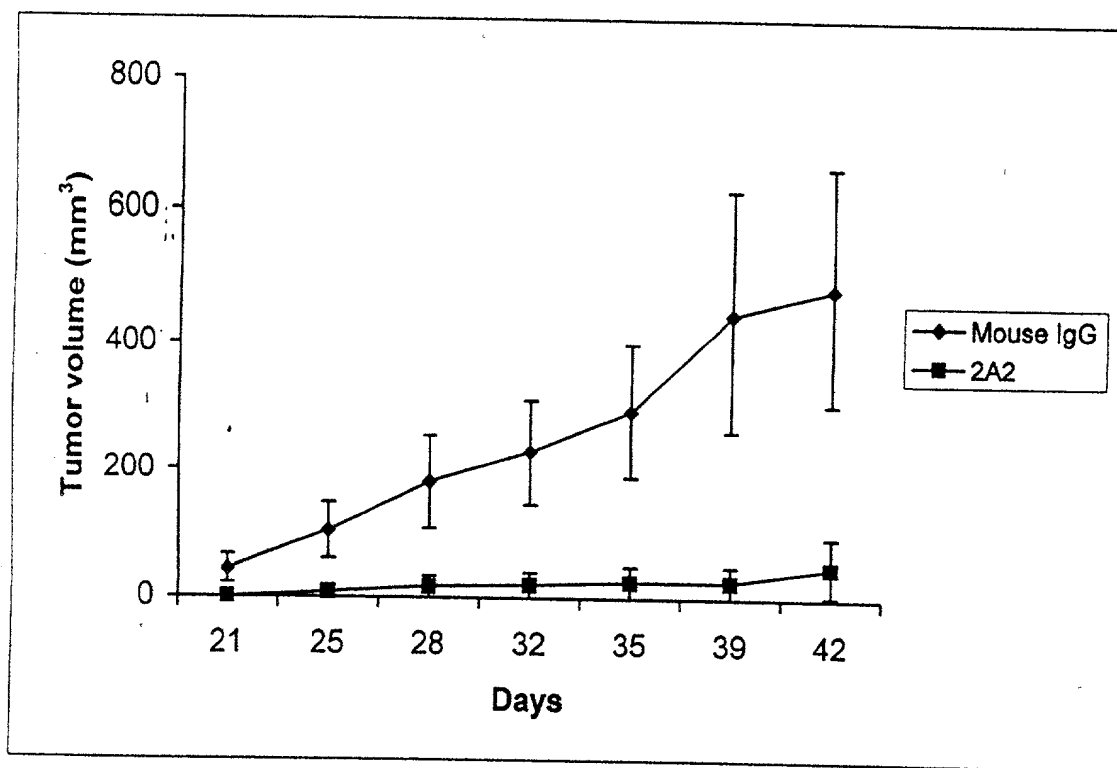


FIG. 56

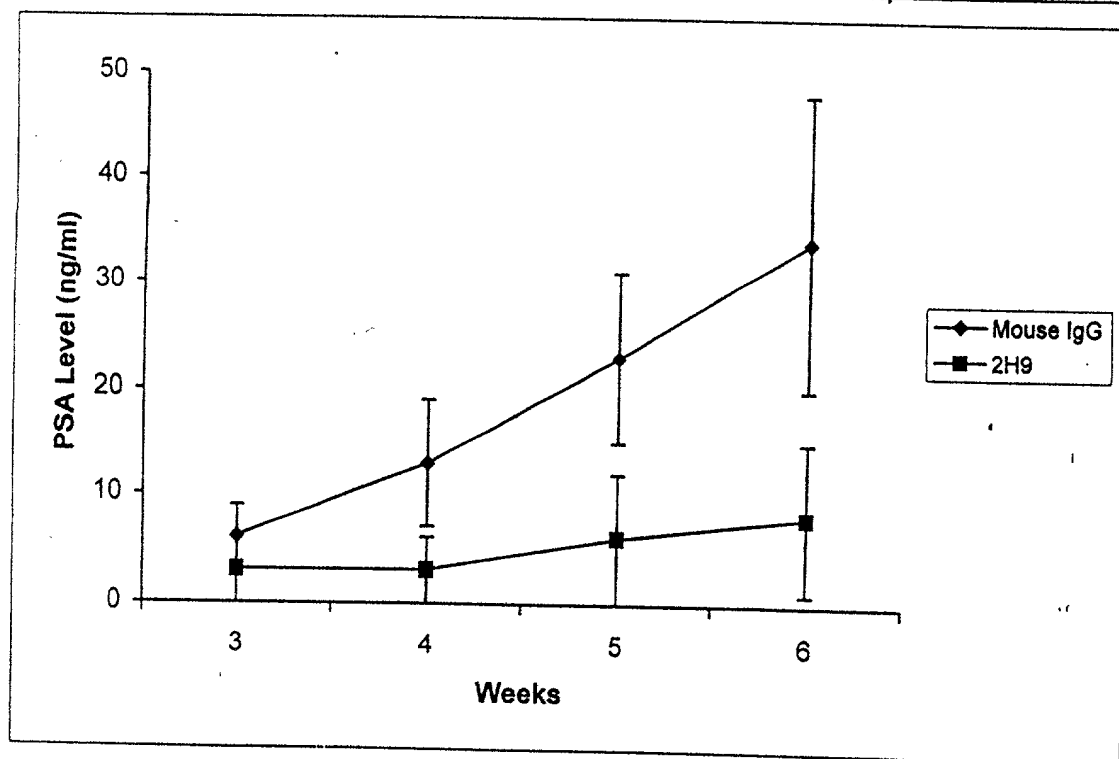
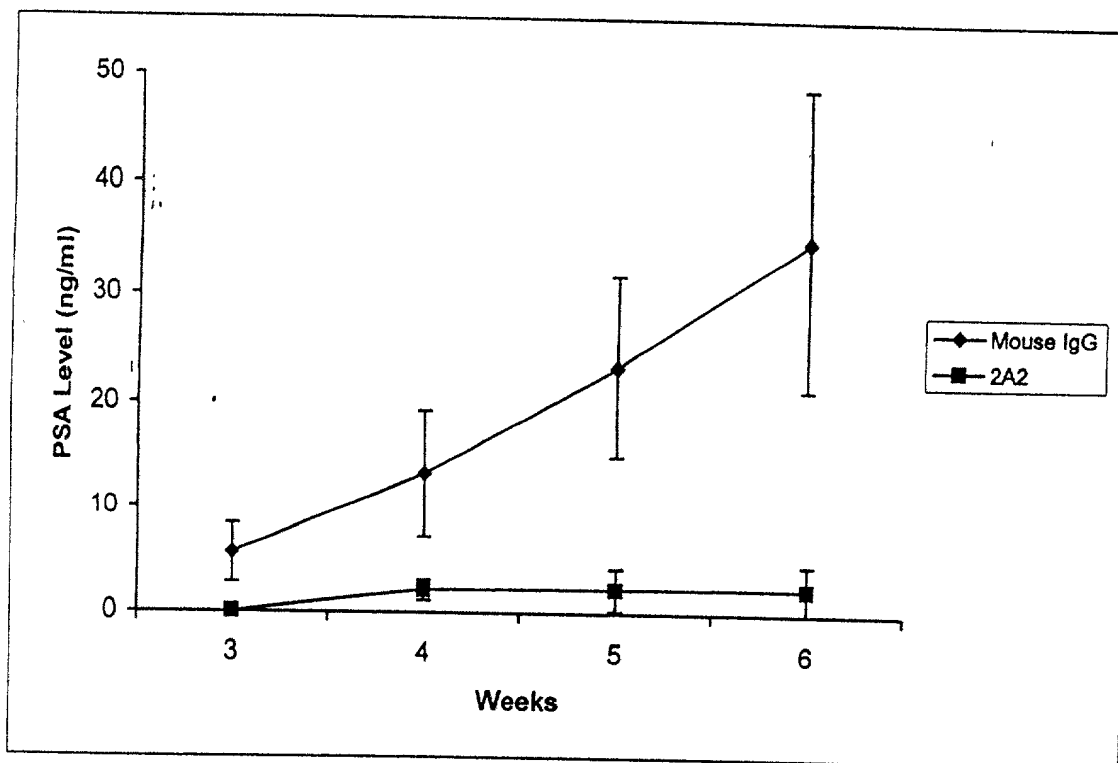


FIG. 57

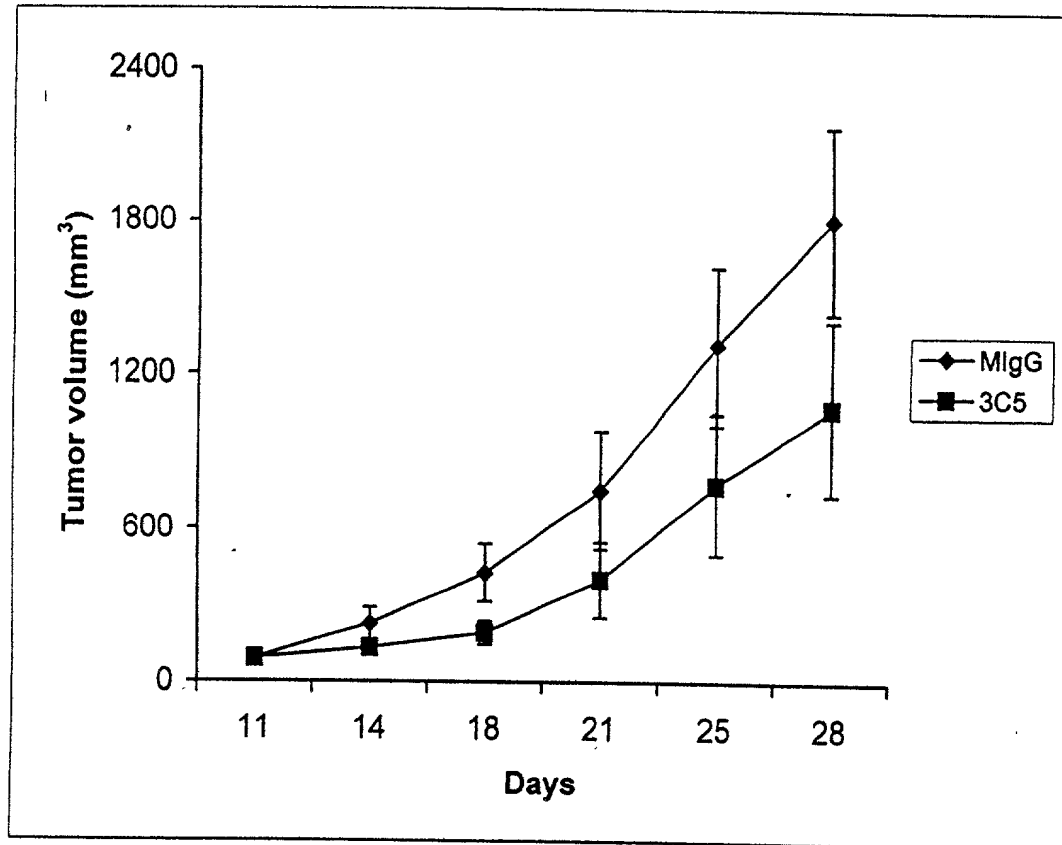


FIG. 58

TGCTTCTTCCTGATGGCAGTGGTTATAGGAGTCAATTCAGAGGTTTCAGCTGCAGCAGTCT 60
C F F L M A V V I G V N S E V Q L Q Q S 20

GGGGCAGAACTTGTGAGGTCAGGGGCCTCAGTCAAGTTGTCCTGCACAGCTTCTGGCTTC 120
G A E L V R S G A S V K L S C T A S G F 40

— CDR1 —
AACATTAAAGACTACTATATACACTGGGTGAATCAGAGGCCTGACCAGGGCCTGGAGTGG 180
N I K D Y Y I H W V N Q R P D Q G L E W 60

— CDR2 —
ATTGGATGGATTGATCCTGAGAATGGTGACACTGAATTTGTCCCGAAGTTCCAGGGCAAG 240
I G W I D P E N G D T E F V P K F Q G K 80

GCCACTATGACTGCAGACATTTTCTCCAACACAGCCTACCTGCACCTCAGCAGCCTGACA 300
A T M T A D I F S N T A Y L H L S S L T 100

— CDR3 —
TCTGAAGACACTGCCGTCTATTACTGTAAAACGGGGGGTTTCTGGGGCCAAGGGACTCTG 360
S E D T A V Y Y C K T G G F W G Q G T L 120

GTCACTGTCTCTGCAGCCAAAACGACACCCCCATCTGTCTATCCACTG
V T V S A A K T T P P S V Y P L

FIG. 58

FIG. 59

TTGGTAGCAACAGCCTCAGATGTCCACTCCCAGGTCCAACCTGCAGCAACCTGGGTCTGAA 60
 L V A T A S D V H S Q V Q L Q Q P G S E 20

CTGGTGAGGCCTGGAACCTCAGTGAAGCTGTCCTGCAAGGCTTCTGGCTATACATTCTCC 120
 L V R P G T S V K L S C K A S G Y T F S 40
 CDR1

AGCTACTGGATGCACTGGGTGAAGCAGAGGCCTGGACAAGGCCTTGAGTGGATTGGAAAT 180
S Y W M H W V K Q R P G Q G L E W I G N 60

ATTGACCCTGGTAGTGGTTACACTAACTACGCTGAGAACCTCAAGACCAAGGCCACACTG 240
I D P G S G Y T N Y A E N L K T K A T L 80
 CDR2

ACTGTAGACACATCCTCCAGCACAGCCTACATGCAGCTCAGCAGCCTGACATCTGAGGAC 300
 T V D T S S S T A Y M Q L S S L T S E D 100

TCTGCAGTCTATTACTGTACAAGCCGATCTACTATGATTACGACGGGATTGCTTACTGG 360
 S A V Y Y C T S R S T M I T T G F A Y W 120
 CDR3

GGCCAAGGGACTCTGGTCACTGTCTCTGCAGCTACAACAACAGCCCCATCTGTCTATCCA 420
 G Q G T L V T V S A A T T T A P S V Y P 160

CTGGCC
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FIG. 59

FIG. 60

AATGACTTCGGGTTGAGCTGGGTTTTTATTATTGTTCTTTTAAAAGGGGTCCGGAGTGAA 60
N D F G L S W V F I I V L L K G V R S E 20

GTGAGGCTTGAGGAGTCTGGAGGAGGCTGGGTGCAACCTGGAGGATCCATGAAACTCTCC 120
V R L E E S G G G W V Q P G G S M K L S 40

TGTGTAGCCTCTGGATTTACTTTTCAGTAATTACTGGATGACTTGGGTCCGCCAGTCTCCA 180
C V A S G F T F S N Y W M T W V R Q S P 60
CDR1

GAGAAGGGGCTTGAGTGGGTTGCTGAAATTCGATTGAGATCTGAAAATTATGCAACACAT 240
E K G L E W V A E I R L R S E N Y A T H 80
CDR2

TATGCGGAGTCTGTGAAAGGGAAATTCACCATCTCAAGAGATGATTCCAGAAGTCGTCTC 300
Y A E S V K G K F T I S R D D S R S R L 100

TACCTGCAAATGAACAACTTAAGACCTGAAGACAGTGGAATTTATTACTGTACAGATGGT 360
Y L Q M N N L R P E D S G I Y Y C T D G 120

CTGGGACGACCTAACTGGGGCCAAGGGACTCTGGTCACTGTCTCTGCAGCCAAAACGACA 420
L G R P N W G Q G T L V T V S A A K T T 140
CDR3

CCCCCATCTGTCTATCCACTGGCCCCTTGTGTA
P P S V Y P L A P C V

104259 224660

FIG. 63

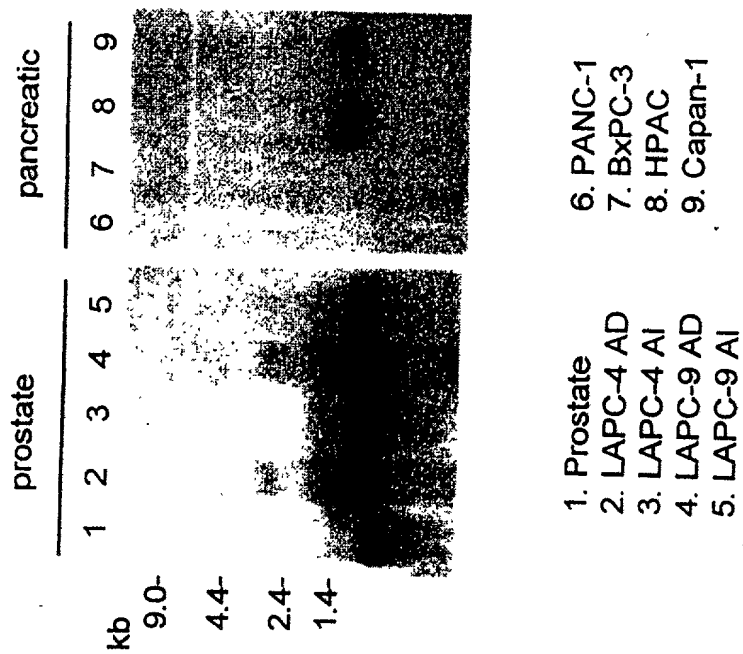
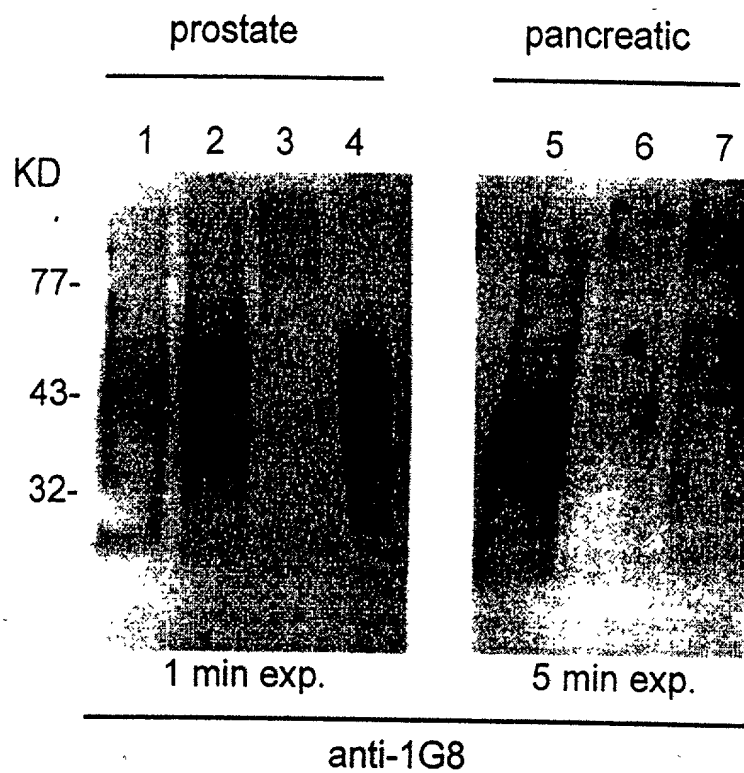


FIG. 64



1. LAPC-4 AD
2. LAPC-9 AI
3. LNCaP
4. LNCaP-PSCA

5. HPAC
6. Capan-1
7. ASPC-1

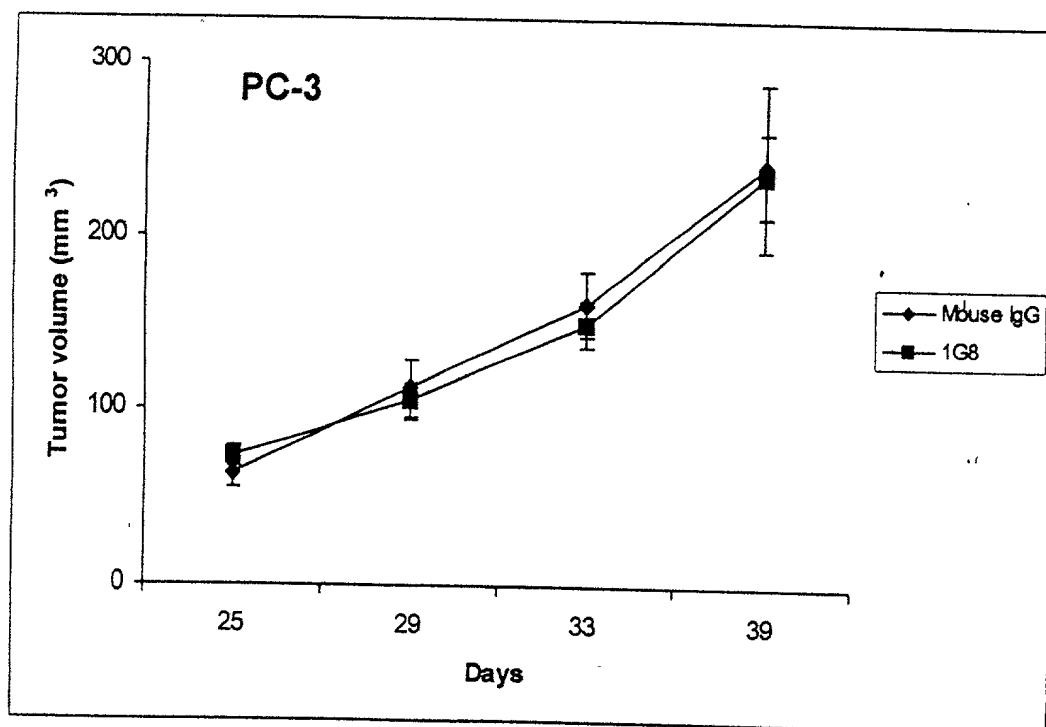
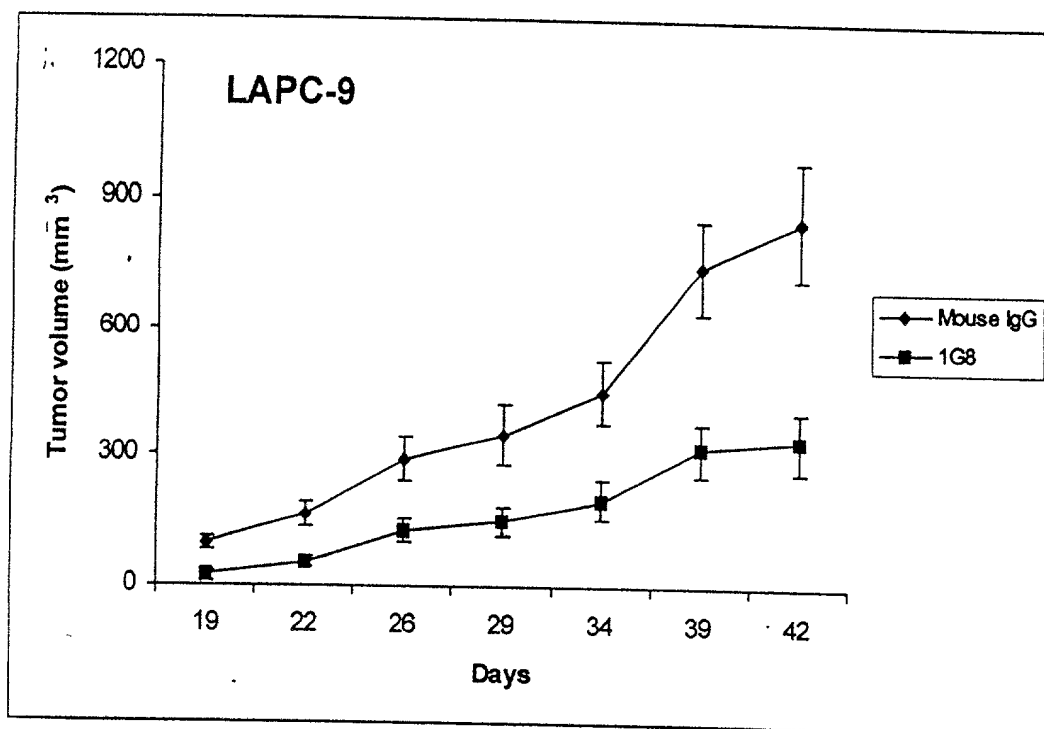
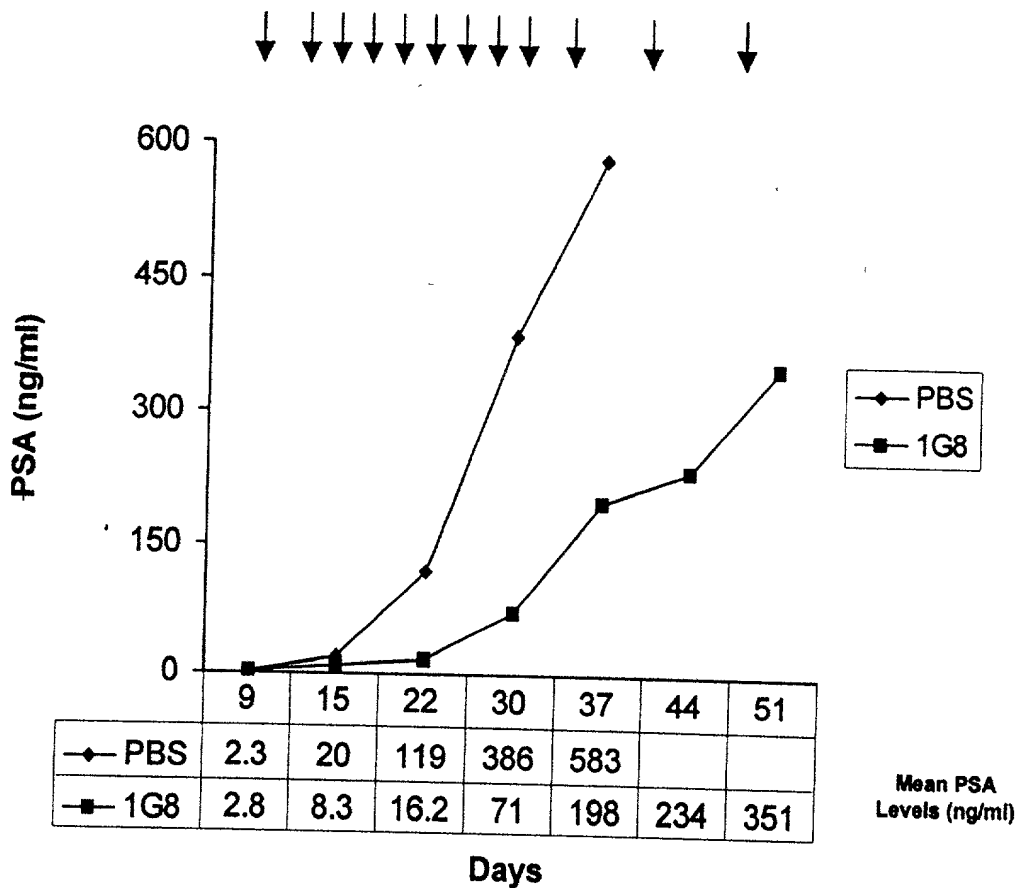


FIGURE 65

A)



B)

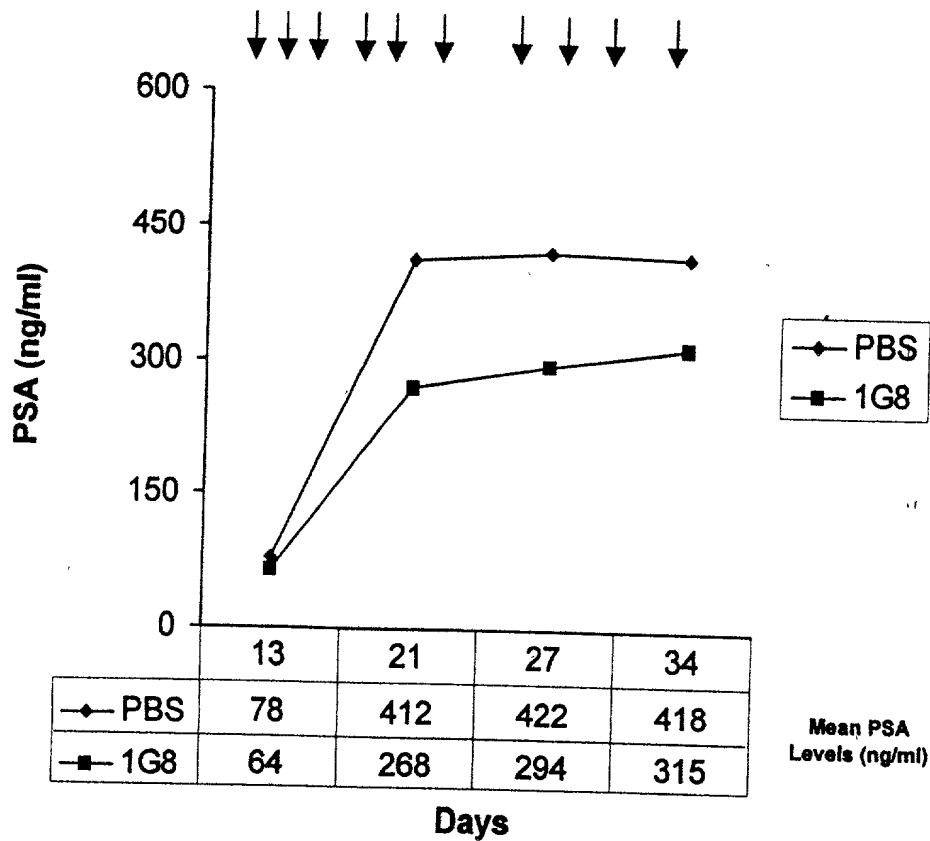
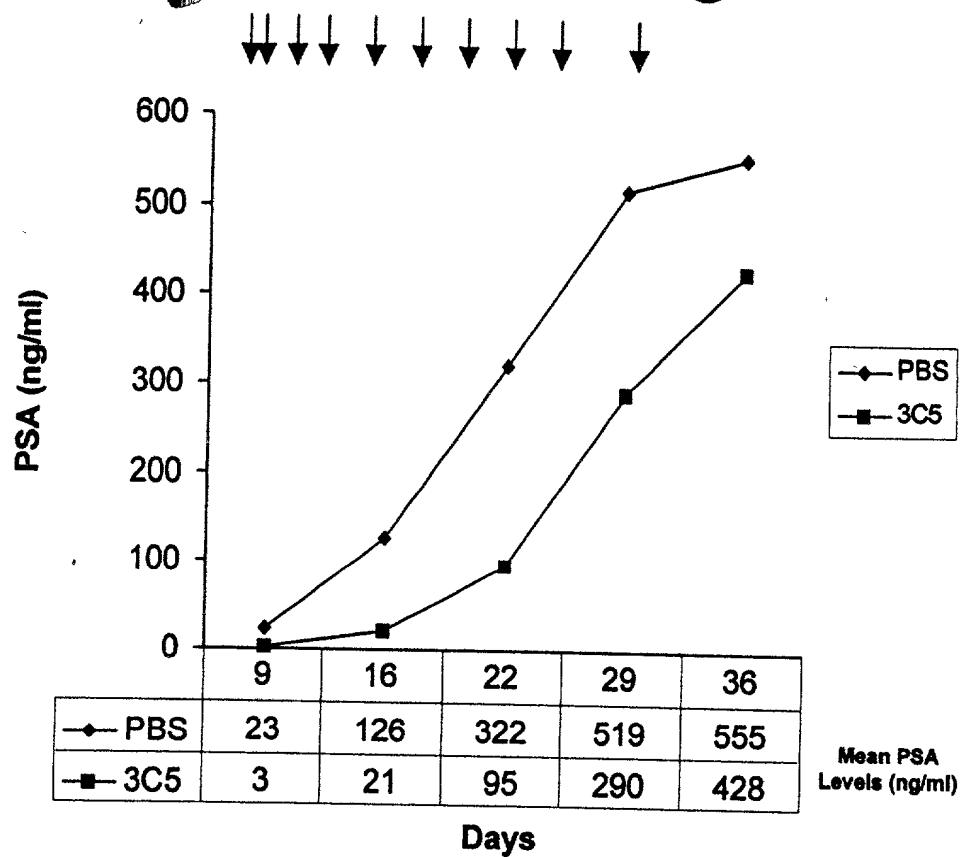


Figure 66

A)



B)

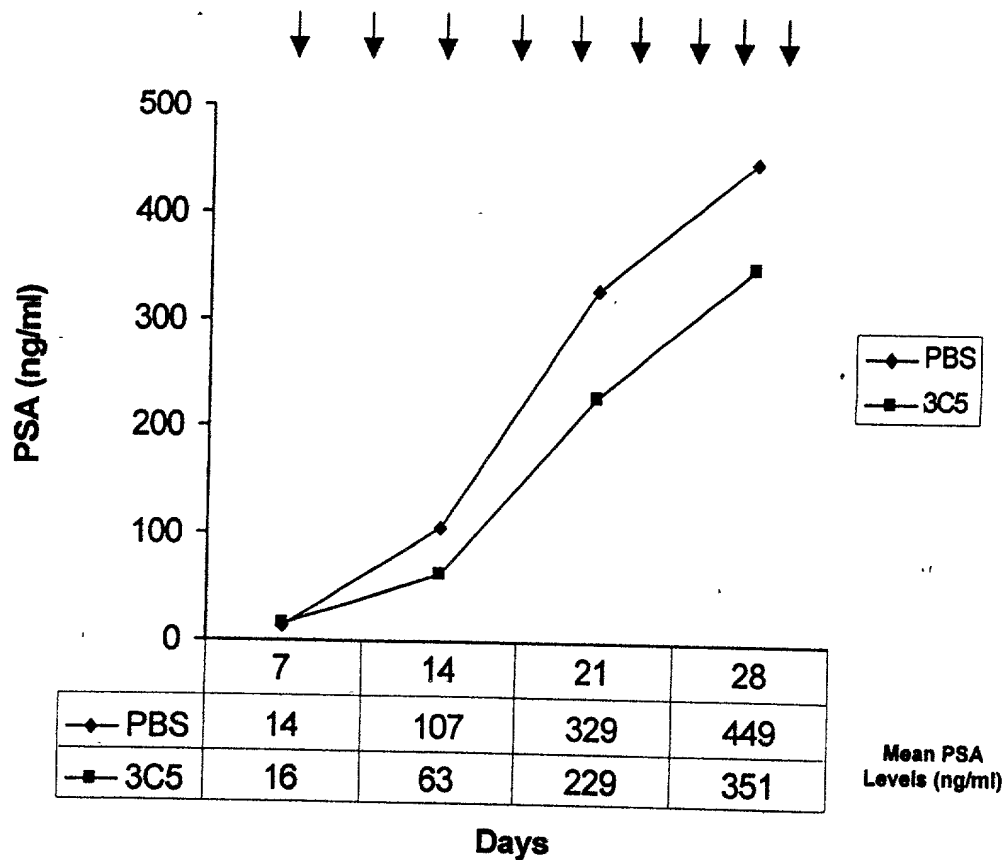
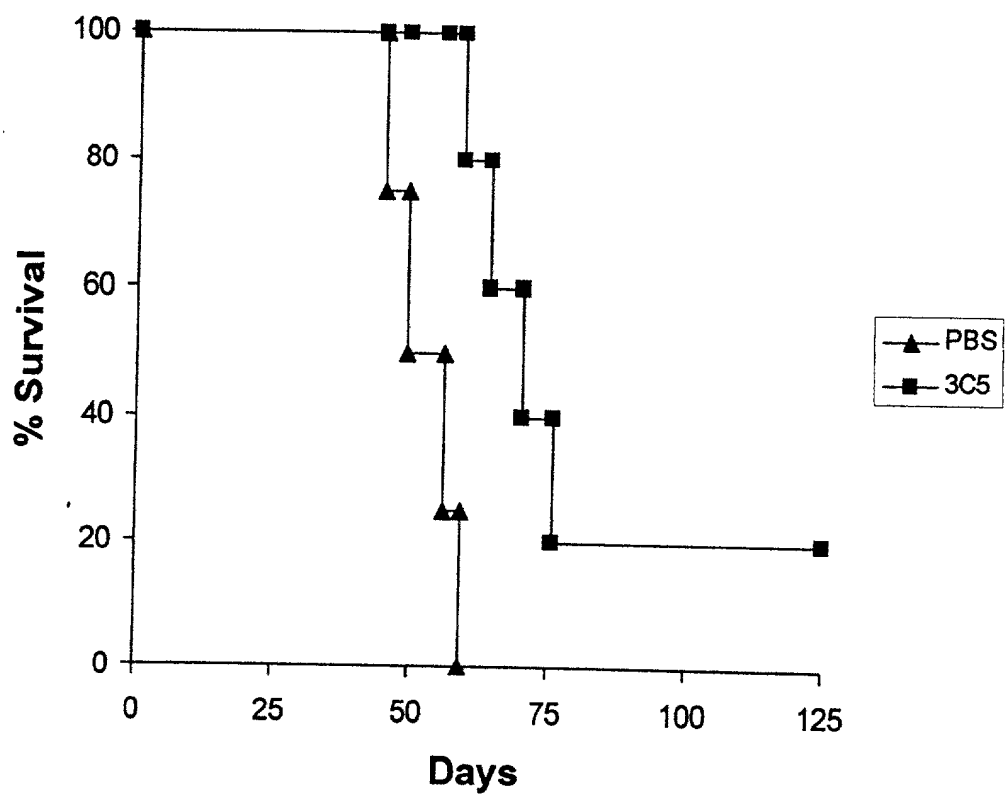


Figure 68

A)



B)

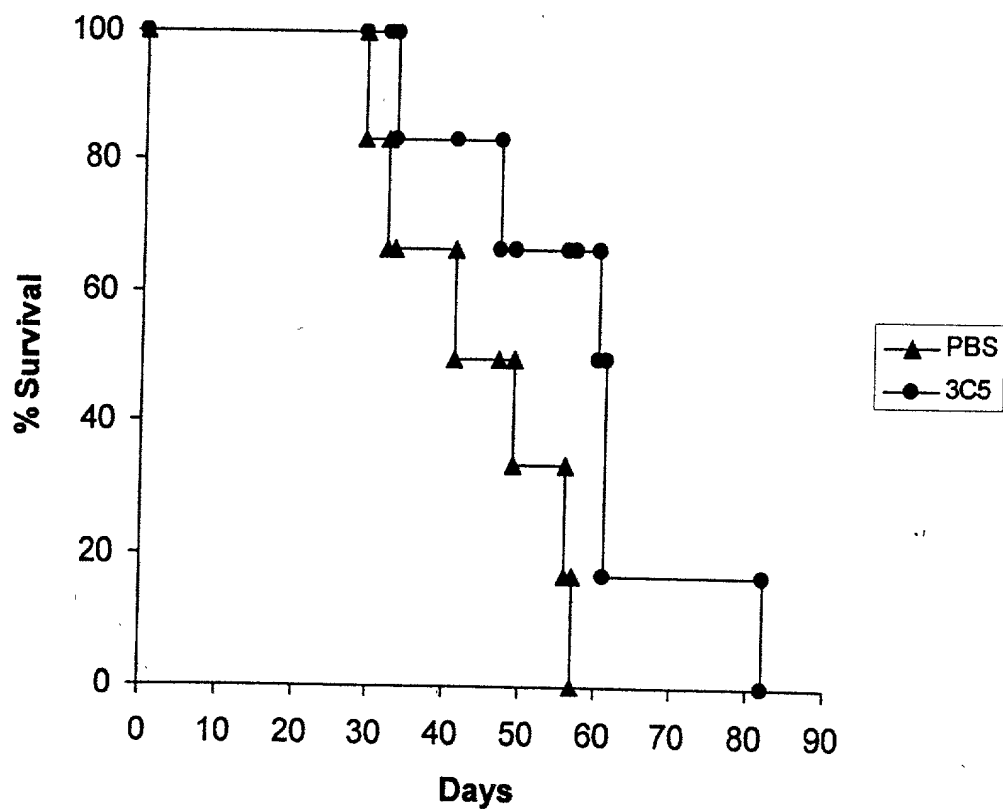


Figure 69

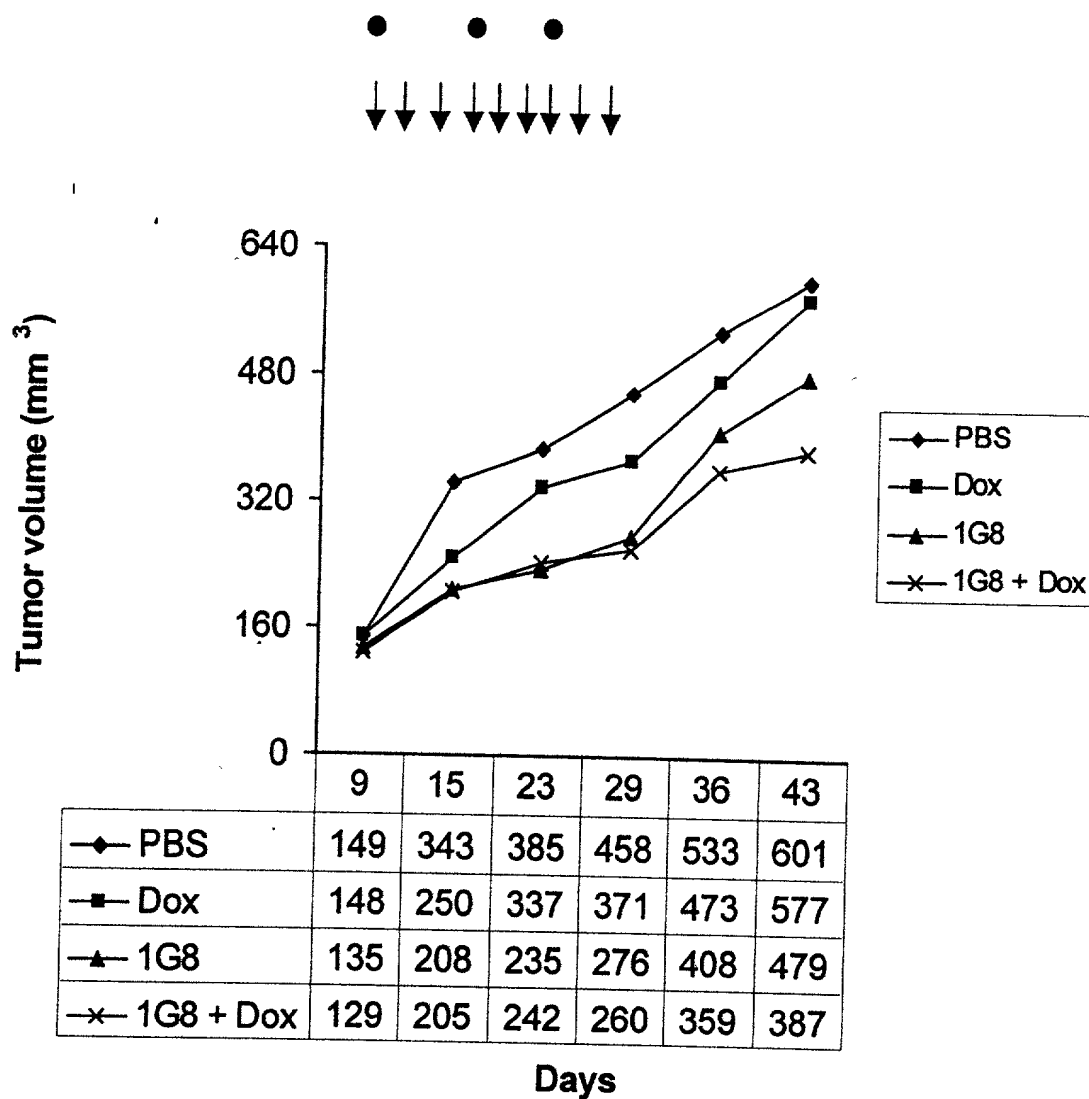
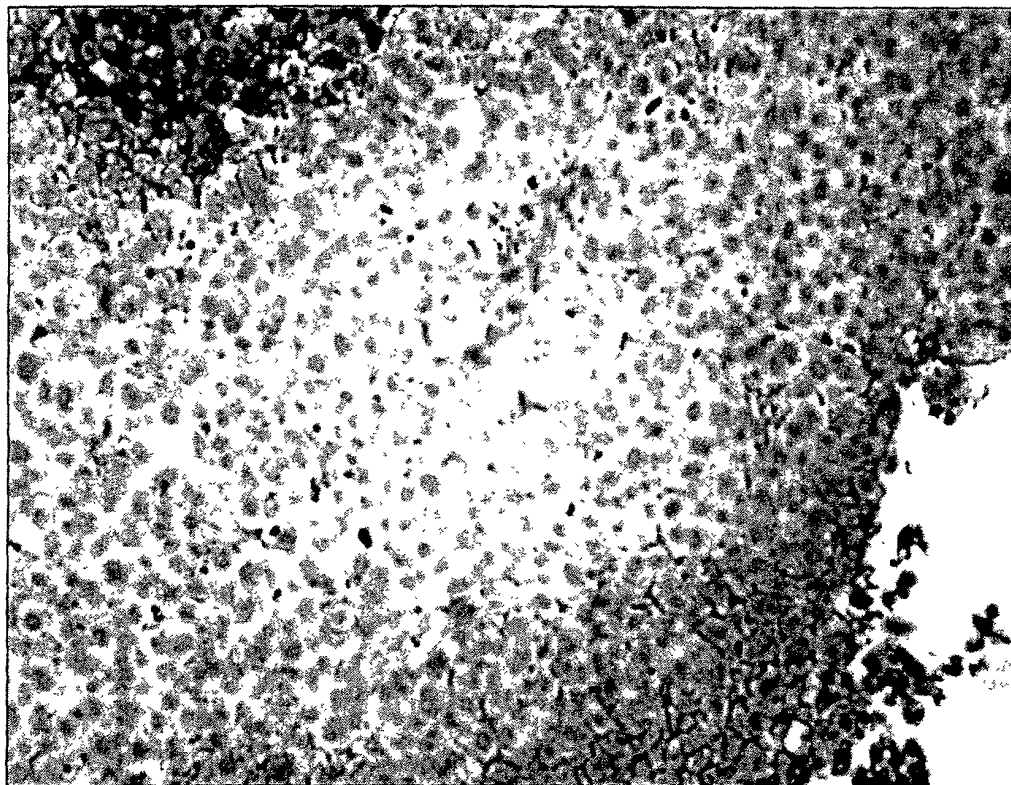


Figure 70

PSCA 3C5 MAb Localizes within LAPC9AD Xenograft Tissue

3C5 Treated



mIgG Treated

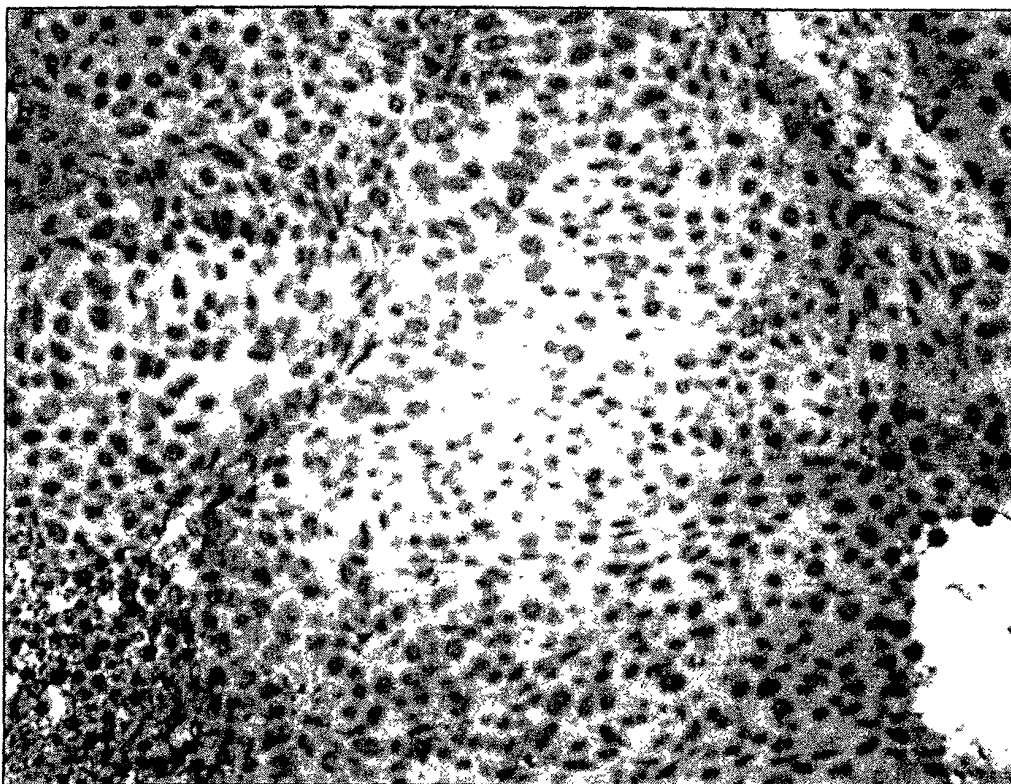


Figure 71

mlgG 3C5

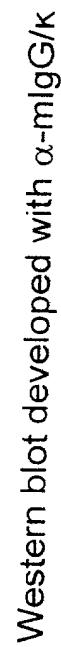
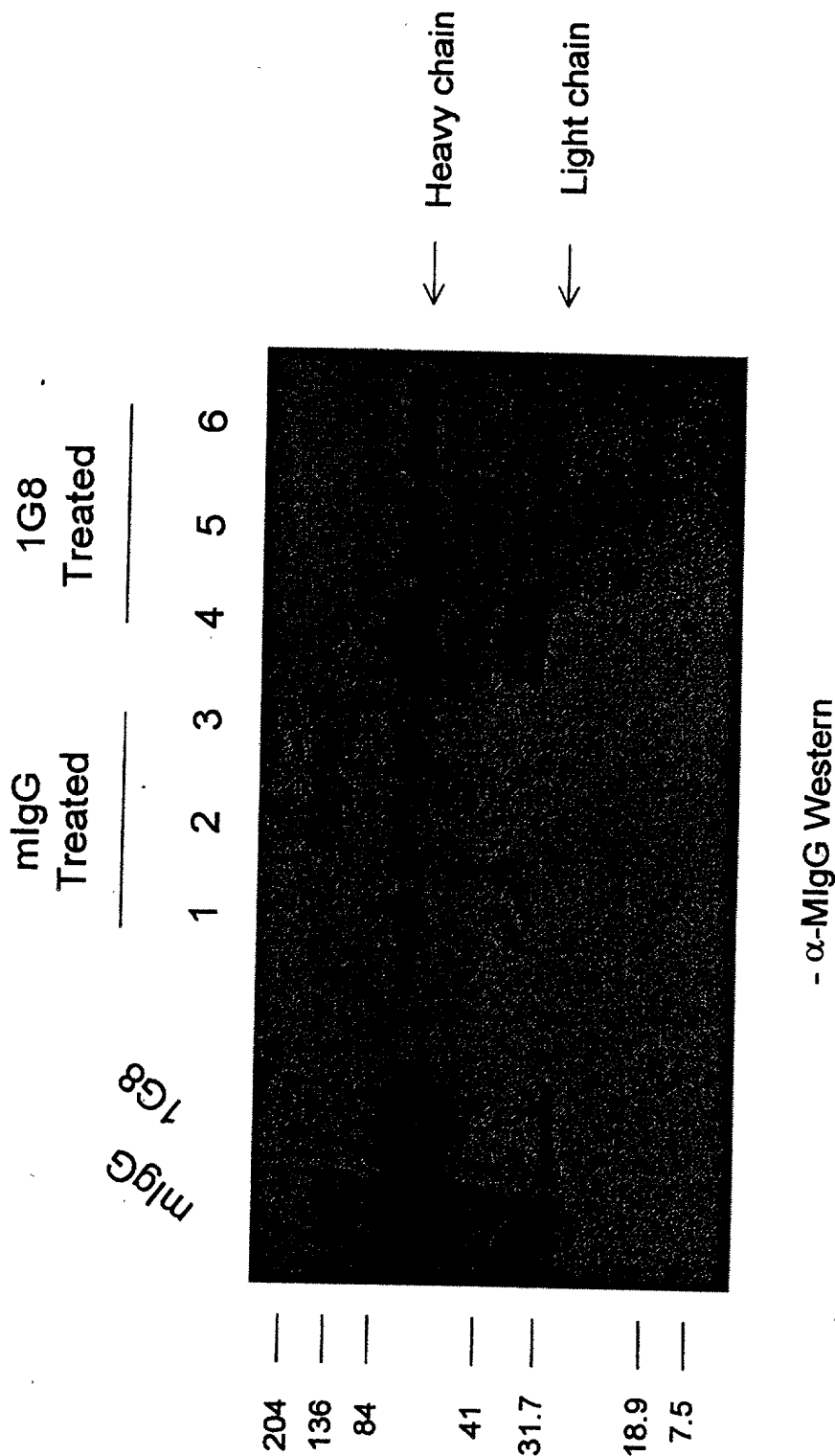


Figure 72

SPECIFIC TARGETING OF THE 1G8 ANTI-PSCA MAb TO ESTABLISHED LAPC-9 TUMORS



Method: Mice bearing established LAPC-9 tumors (>100 mm³) were injected with either mlgG or the anti-PSCA MAb 1G8. Tumors were harvested a week later and made into protein lysates for Western analysis.

Figure 73